Supporting Information

An Electrochemical Azidation of Least Hindered Tertiary and Benzylic C(sp^3)-H Bonds

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Content

1. Reagents

All commercial materials were used as received unless otherwise noted. Superdry solvents and deuterated solvents were purchased from Energy Chemical. Starting materials for this study were purchased from Leyan or were synthesized according to reported procedures.

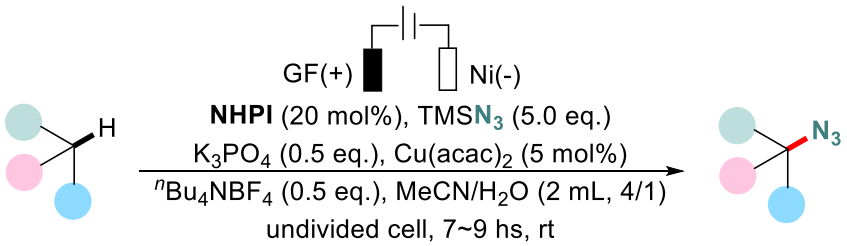
TLC were performed on silica gel Leyan HSGF254 plates and visualization of the developed chromatogram was performed by fluorescence quenching (λmax = 254 nm). Flash chromatography was performed using silica gel (200-300 mesh) purchased from Shanghai Haohong Scientific Co., Ltd.

2. Instruments

NMR spectra were recorded on Bruker AVANCE AV 500 instruments, and all NMR experiments were reported in units, parts per million (ppm), using residual solvent peaks as internal reference. Multiplicities are recorded as: s = singlet, d = doublet, t = triplet, dd = doublet of doublets, td = triplet of doublets, br = broad singlet, m = multiplet. Mass spectra were determined on a Hewlett-Packard 5988A spectrometer by direct inlet at 70 eV. High-resolution mass spectrometry (HRMS) data were obtained on an LC-MS instrument (ESI-HRMS, Agilent 6520 Q-TOF LC/MS). All reactions were carried out in a 5 ml flat mouth test tube.

3. General Procedure

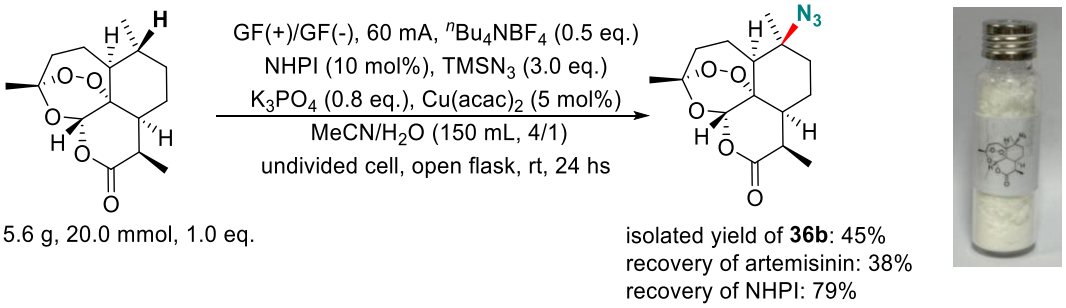
3.1 Electrochemical azidation of C(sp^3)-H bond



The 5 mL flat mouth test tube was equipped with two rubber plugs. A graphite felt (1

cm x 1.5 cm x 0.5 cm) and a nickel sheet (1 cm x 1 cm x 0.2 cm) were used as anode and cathode, respectively. The graphite felt anode is attached to a platinum wire. Substrate (0.5 mmol, 1.0 equiv), K_3PO_4 (0.5 equiv), $Cu(acac)_2$ (5 mol%), NHPI (0.1 mmol, 20 mol%) were first dissolved in CH_3CN/H_2O (2.0 mL, 4/1) and stirred for 5 min at room temperature. Then the mixture was added with Bu_4NBF_4 (0.5 equiv). The reaction mixture was stirred and electrolyzed with a constant current of 10 mA at room temperature (23 °C). Upon completion, the reaction mixture was extracted with DCM (3 x 2.0 mL). The combined organic solution was dried over anhydrous Na_2SO_4. Then the mixture was filtered and concentrated. The residue was purified by chromatography on silica gel to afford the desired product. **Please note: HN_3 may produce.**

3.2 Gram-scale experiment:

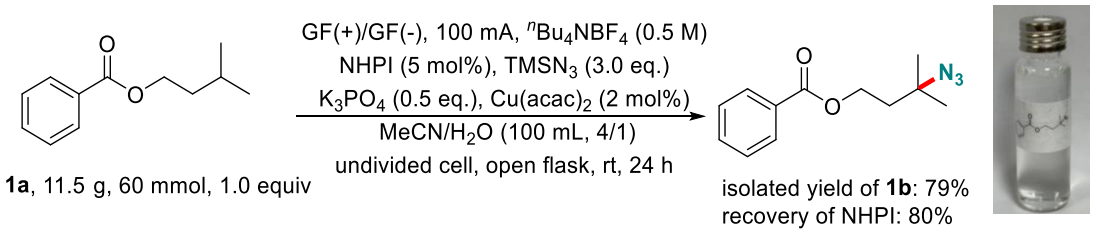


36a, 5.6 g, 20.0 mmol, 1.0 eq.

isolated yield of **36b**: 45%
recovery of artemisinin: 38%
recovery of NHPI: 79%

Put two graphite felts (6 cm x 6 cm x 0.5 cm) as both cathode and anode in a 300 mL of beaker. The graphite felt electrodes are attached to a platinum wire. Substrate **36a** (5.6 g, 20.0 mmol, 1.0 equiv.) and NHPI (10 mol%) were first dissolved in CH_3CN/H_2O (150.0 mL, 4/1, v/v) and stirred for 10 min at room temperature. Then the mixture was added with Bu_4NBF_4 (0.5 equiv.), K_3PO_4 (0.8 equiv.) and $Cu(avac)_2$ (5 mol%). Finally, $TMSN_3$ (1.0 equiv.) was added dropwise in multiple portions every 3 h. The reaction mixture was stirred and electrolyzed with a constant current of 60 mA at room temperature for 24 h. After the reaction was completed, as monitored with TLC, the solvents were removed in *vacuo,* and the residue was purified by silica gel flash chromatography to give the desired products **36b** (2.91 g, 45 %). It is worth

noting that the recovery rate of NHPI is 79 %. **Please note: HN_3 may produce.**



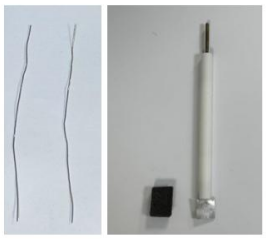
1a, 11.5 g, 60 mmol, 1.0 equiv

isolated yield of **1b**: 79%
recovery of NHPI: 80%

Put two graphite felts (6 cm x 6 cm x 0.5 cm) as both cathode and anode in a 300 mL beaker. The graphite felt electrodes are attached to a platinum wire. Substrate **1a** (11.5 g, 60.0 mmol, 1.0 equiv.) and NHPI (5 mol%) were first dissolved in CH_3CN/H_2O (100.0 mL, 4/1, v/v) and stirred for 10 min at room temperature. Then the mixture was added with Bu_4NBF_4 (0.5 M), K_3PO_4 (0.5 equiv.), and $Cu(acac)_2$ (2 mol%). Finally, $TMSN_3$ (1.0 equiv.) was added dropwise in multiple portions every 3 h. The reaction mixture was stirred and electrolyzed with a constant current of 100 mA at room temperature for 24 hs. After the reaction was completed as monitored with TLC, the solvents were removed in *vacuo,* and the residue was purified by silica gel flash chromatography to give the desired products **1b** (11.0 g, 79 %). It is worth noting that the recovery rate of NHPI is 80 %. **Please note: HN_3 may produce.**

Note: The two graphite felts should be avoided from direct contact during the reaction.

4. The Reaction Device Photographs



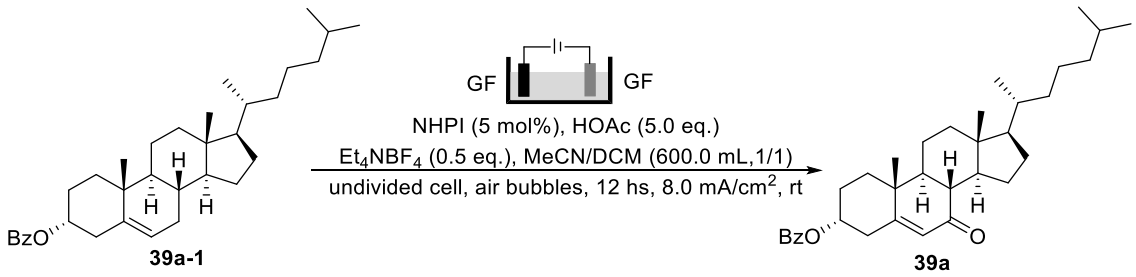
Platinum wire: 0.5 mm x 8 cm

Graphite felt: 1.0 cm x 1.5 cm x 0.5 cm

Figure 1. Undivided cell for current controlled electrolysis

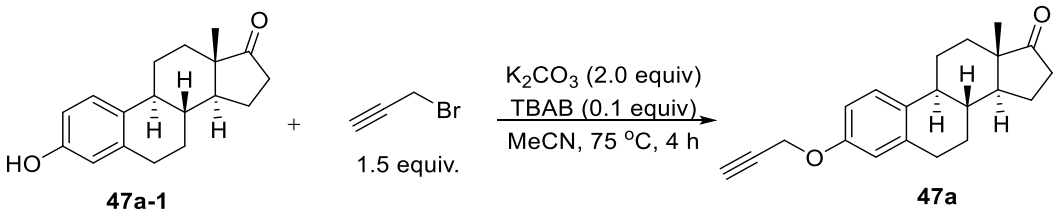
5. Synthesis of substrates

5.1 Synthesis of compound 39a



Put two graphite felts (10 cm x 10 cm x 0.5 cm) as both cathode and anode in a 1000 mL plastic bucket. The graphite felt electrodes are connected to a platinum wire. These two electrodes were connected to a DC-regulated power supply. The distance between the graphite felt electrodes is 8.0 cm. A booster pump was attached to the plastic bucket via a plastic pipe to provide enough air bubbles. Et_4NBF_4 (0.5 equiv.) was first dissolved in MeCN/DCM (600.0 mL, 1/1) and stirred for 10 min at room temperature. Then the mixture was added with **39a-1** (0.25 mol, 1.0 equiv.), NHPI (5 mol%) and HOAc (5.0 equiv.). The reaction mixture was electrolyzed with a constant current of 800 mA at room temperature (23 ^oC). After the reaction completed as monitored with TLC, the reaction mixture was extracted with DCM (3 x 100 mL), the combined organic phase was washed with brine, and dried over Na_2SO_4. Then the mixture was filtered and concentrated. The residue was purified by chromatography on silica gel to afford the desired product **39a** (white solid, 80.6 g, 64 %). The spectroscopic data were consistent with those previously reported in the literature.[1]

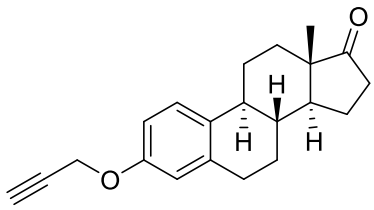
5.2 Synthesis of compound 47a



A 100 mL round-bottom flask was charged with estrone (**47a-1,** 10 mmol, 1.0 equiv.), K_2CO_3 (2.8 g, 20.0 mmol, 2 equiv.), TBAB (0.1 equiv.) and 20.0 mL MeCN. Then a

solution of 3-Bromopropyne (15.0 mmol, 1.5 equiv.) in 10.0 mL of MeCN was added dropwise to the mixture at room temperature. After being stirred for 30 min at room temperature, the reaction mixture was stirred for 4 h at 75 °C. The reaction was cooled to room temperature and filtered, then diluted with water (30 mL) and extracted with EtOAc three times (3 x 10 mL). The organic phase was separated and eventually dried over anhydrous Na_2SO_4. Solvent was removed in *vacuo*. The crude residue was purified by flash column chromatography on silica gel to afford the target compound **47a** (2.59 g, 84% yield).

(8*R*,9*S*,13*S*,14*S*)-13-methyl-3-(prop-2-yn-1-yloxy)-6,7,8,9,11,12,13,14,15,16-decahydro-17H-cyclopenta[a]phenanthren-17-one

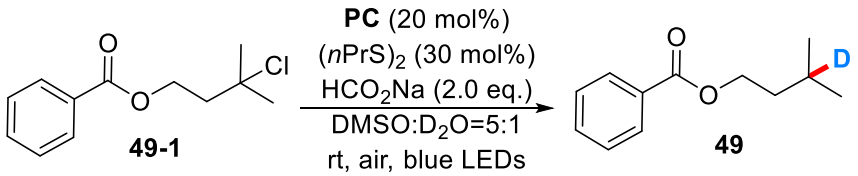


47a

R_f = 0.4, 20% acetone in hexane, white solid (2.59 g, 84 % yield)

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.21 (d, J = 8.5 Hz, 1H), 6.78 (d, J = 6.2 Hz, 1H), 6.71 (s, 1H), 4.65 (s, 2H), 2.96 – 2.85 (m, 2H), 2.56 – 2.44 (m, 2H), 2.38 (d, J = 12.0 Hz, 1H), 2.24 (t, J = 8.2 Hz, 1H), 2.18 – 2.09 (m, 1H), 2.08 – 1.99 (m, 2H), 1.95 (d, J = 11.5 Hz, 1H), 1.59 (dd, J = 27.8, 15.8 Hz, 2H), 1.53 – 1.41 (m, 4H), 0.90 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 220.73, 155.53, 137.80, 132.94, 126.31, 114.94, 112.32, 78.84, 75.40, 55.70, 50.36, 47.94, 43.94, 38.26, 35.82, 31.56, 29.62, 26.48, 25.86, 21.56, 13.83. **HRMS (ESI-TOF) m/z:** $[M+H]^+$ Calcd for $C_{21}H_{25}O_2$ 309.1849; Found: 309.1849.

5.3 Synthesis of compound 49



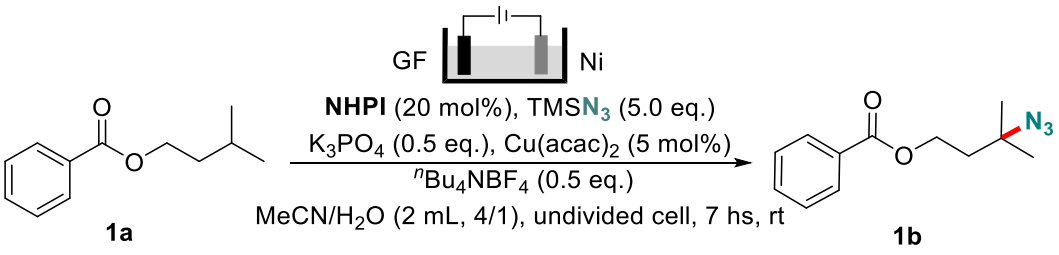
A dried 5 mL glass vial was charged with **49-1** (45.2 mg, 0.20 mmol, 1.0 equiv), *N*-ethyl-3,6-bis(dimethylamino)carbazole (**PC**) (11.2 mg, 0.040 mmol, 20 mol%),

(nPrS)$_2$ (0.060 mmol, 30 mol%), HCO_2Na (0.40 mmol, 2.0 equiv), D_2O (0.2 mL) and DMSO (1.0 mL) under air and then performed in a sealed vessel. The glass vial was positioned approximately 3 cm away from a 50 W blue LED lamp (max = 400 nm). After being stirred at room temperature for 72 h, the reaction mixture was purified by flash chromatography to afford, as a yellowish oil **49** (28.0 mg, 73% yield, 81% D). The spectroscopic data of **49** were consistent with those previously reported in the literature.[2]

6. Optimization studies

All screening reactions were carried out at a 0.5 mmol scale in a 5 mL flat mouth test tube unless otherwise noted. Isoamyl Benzoate **1a** (96.1 mg, 0.5 mmol, 1.0 equiv), other specified reagents, and a magnetic stir bar were added to a 5 mL flat mouth test tube. The graphite felt (1 cm x 1.5 cm x 0.5 cm) and nickel sheet are used as anode and cathode, respectively. The graphite felt (GF) anode is attached to a platinum wire. The constant current electrolysis was carried out at room temperature. Upon completion, the reaction mixture was extracted with DCM (3 x 2.0 mL). The combined organic solution was dried over anhydrous Na_2SO_4. Then the mixture was filtered and concentrated. The residue was purified by chromatography on silica gel to afford the desired product.

Note: The graphite felt (GF) differs dramatically from the graphite rod in the aspects of original material, manufacturing process, structure, and properties.[3]



Entry	Deviation from standard conditions	yield of 1b(%)[b]	RSM (%)[c]

1	none	80	<10
2	MeCN/H_2O (5 mL, 4/1), 15 hs	73	<10
3	MeOH or HFIP as solvent	trace	>90
4	Pt as cathode	70	<10
5	GF as cathode	54	23
6	Et_4NBF_4 instead of nBu_4NBF_4	69	<10
7	TsN_3 or NaN_3 instead of $TMSN_3$	trace	>90
8	I= 5 mA	43	39
9	I= 15 mA	71	<10
10	no K_3PO_4	16	72
11	no $Cu(acac)_2$	46	39
12	no NHPI	trace	>90
13	No electricity	0	100

[a] Reaction conditions: 0.5 mmol of substrate, 20 mol% of NHPI, 5.0 equiv of $TMSN_3$, 0.5 equiv of K_3PO_4, 20 mol% of $Cu(acac)_2$, 0.5 equiv of Bu_4NBF_4, solvent (2 mL), graphite felt (1.0 cm × 1.5 cm × 0.5 cm), Ni plate cathode (1.0 cm × 1.0 cm × 0.2 mm), room temperature, 7 hs, 2.61 F/mol, η=31%. [b] Isolated yield. [c] RSM is the short for recovery of starting material.

6.1 Calculation of Faradaic efficiency

The faradaic efficiency of the reaction was calculated using the follow formula[1]

$$\eta = \frac{Q_{theo}}{Q_{exp}} \quad (1)$$

Where,

$$Q_{theo} = Z_p \cdot N_p \cdot F$$

$$Q_{exp} = I \cdot t = Z \cdot N \cdot F \cdot equiv.$$

$$\eta = \frac{Z_p \cdot N_p \cdot F}{Z \cdot N \cdot F \cdot equiv.} = \frac{Y}{equiv.}$$

η: faradaic efficiency in percent [%]; Q_{theo}: theoretical charge in Coulomb [C]; Q_{exp}: experimental charge in Coulomb [C]; equiv.: electron equivalents (F/mol or equiv.); Z_p :number of electrons per product [-]; N_p: number of moles of the product [mol]; Y: yield in percent [%].

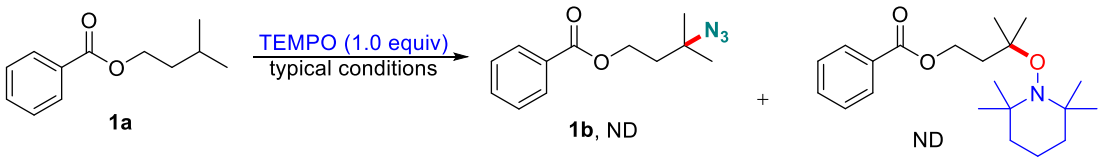
Here, Y=80%, equiv.=2.61 F/mol

The faradaic efficiency was calculated using eq 1:

$$\eta = \frac{Z_p \cdot N_p \cdot F}{Z \cdot N \cdot F \cdot equiv.} = \frac{Y}{equiv.} = \frac{80\%}{2.61} = 31\%$$

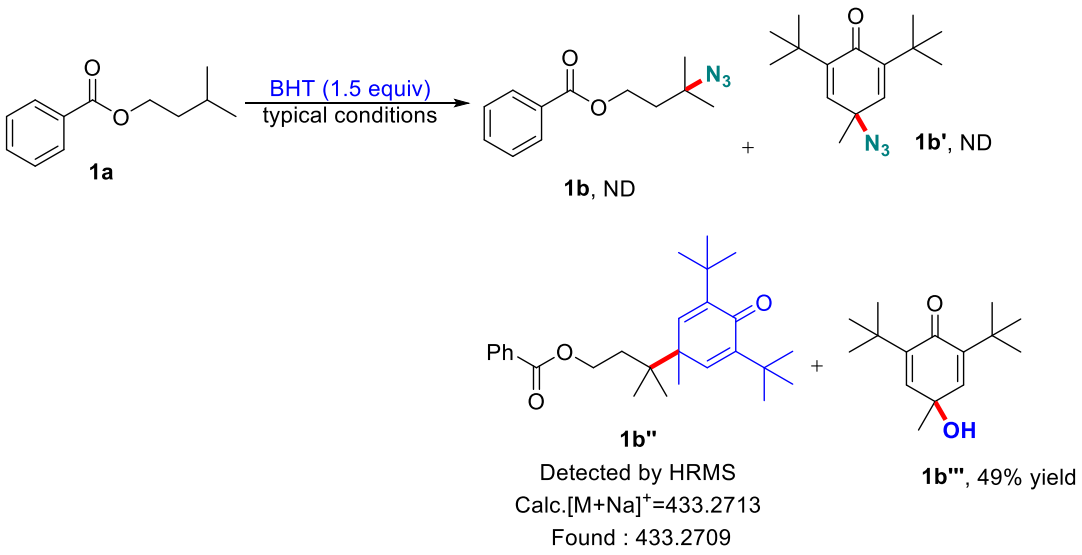
7. Mechanistic studies

7.1 Spin trapping experiment with TEMPO



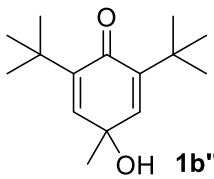
The 5 mL flat mouth test tube was equipped with two rubber plugs. A graphite felt (1 cm x 1.5 cm x 0.5 cm) and a nickel sheet (1 cm x 1 cm x 0.2 cm) were used as anode and cathode, respectively. The graphite felt anode is attached to a platinum wire. Substrate (0.5 mmol, 1.0 equiv), K_3PO_4 (0.5 equiv), $Cu(acac)_2$ (5 mol%), NHPI (0.1 mmol, 20 mol%) were first dissolved in CH_3CN/H_2O (2.0 mL, 4/1) and stirred for 5 min at room temperature. Then the mixture was added with TEMPO (1.0 equiv.) and Bu_4NBF_4 (0.5 equiv). The reaction mixture was stirred and electrolyzed with a constant current of 10 mA at room temperature (23 °C) for 9 h. During this process, we monitored the reaction using TLC and did not observe the formation of compound **1b**, nor did we monitor the free radical-trapping adduct of TEMPO; the raw materials are basically not converted.

7.2 Spin trapping experiment with BHT



The 5 mL flat mouth test tube was equipped with two rubber plugs. A graphite felt (1 cm x 1.5 cm x 0.5 cm) and a nickel sheet (1 cm x 1 cm x 0.2 cm) were used as anode and cathode, respectively. The graphite felt anode is attached to a platinum wire. Substrate (0.5 mmol, 1.0 equiv), K_3PO_4 (0.5 equiv), $Cu(acac)_2$ (5 mol%), NHPI (0.1 mmol, 20 mol%) were first dissolved in CH_3CN/H_2O (2.0 mL, 4/1) and stirred for 5 min at room temperature. Then the mixture was added with BHT (1.5 equiv.) and Bu_4NBF_4 (0.5 equiv). The reaction mixture was stirred and electrolyzed with a constant current of 10 mA at room temperature (23 °C) for 9 h. Upon completion, the reaction mixture was extracted with DCM (3 x 2.0 mL). The combined organic solution was dried over anhydrous Na_2SO_4. Then the mixture was filtered and concentrated. The residue was purified by silica gel flash chromatography (eluted with hexane/acetone (v/v 100:1)) to give the product **1b'''**. Product compound **1b** and **1b'** is not observed. The corresponding product of radical trapping **1b''** was detected by HR-MS (positive mode ESI).

2,6-di-*tert*-butyl-4-hydroxy-4-methylcyclohexa-2,5-dien-1-one (1b''')



1b''' R_f = 0.3, 5% acetone in hexane, yellowish oil (86.0 mg, 49% yield)

^{1}H NMR (500 MHz, $CDCl_3$) δ 6.56 (s, 2H), 1.76 (s, 1H), 1.42 (s, 3H), 1.22 (s, 18H).[4]

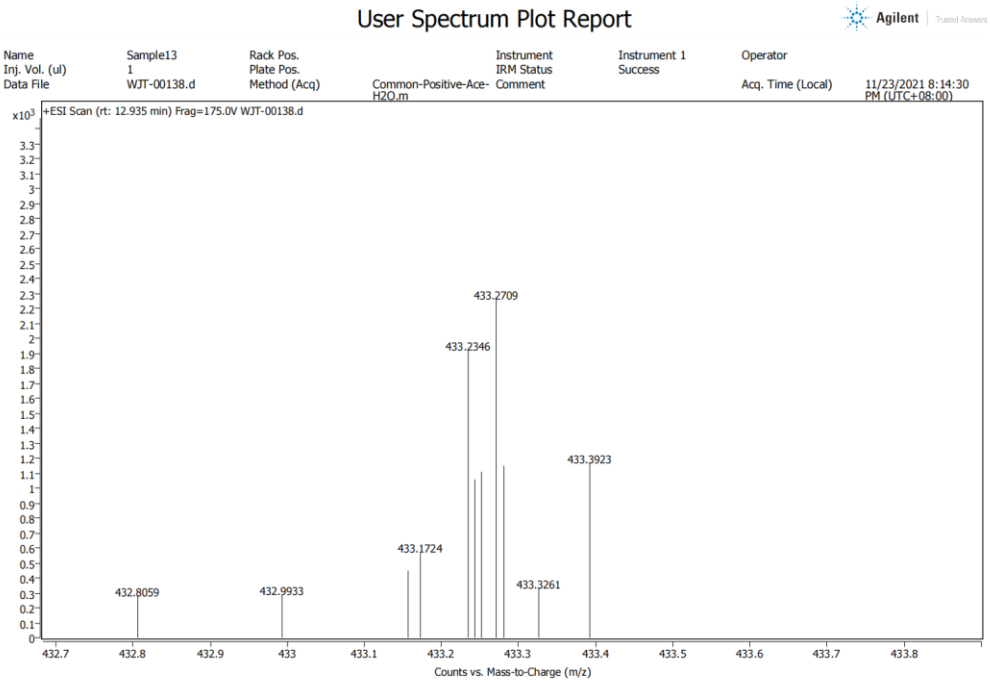
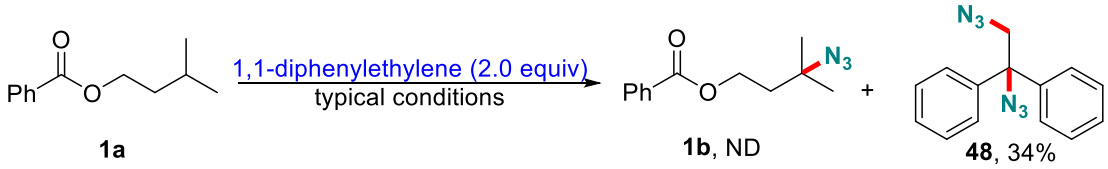


Figure 2 HR-ESI mass spectra of **1b''**

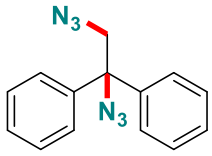
7.3 Spin trapping experiment with 1,1-diphenylethylene



The 5 mL flat mouth test tube was equipped with two rubber plugs. A graphite felt (1 cm x 1.5 cm x 0.5 cm) and a nickel sheet (1 cm x 1 cm x 0.2 cm) were used as anode and cathode, respectively. The graphite felt anode is attached to a platinum wire. Substrate (0.5 mmol, 1.0 equiv), K_3PO_4 (0.5 equiv), $Cu(acac)_2$ (5 mol%), NHPI (0.1 mmol, 20 mol%) were first dissolved in CH_3CN/H_2O (2.0 mL, 4/1) and stirred for 5 min at room temperature. Then the mixture was added with 1,1-diphenylethylene (2.0 equiv.) and Bu_4NBF_4 (0.5 equiv). The reaction mixture was stirred and electrolyzed with a constant current of 10 mA at room temperature (23 °C) for 9 h. Upon completion, the reaction mixture was extracted with DCM (3 x 2.0 mL). The combined organic solution was dried over anhydrous Na_2SO_4. Then the mixture was

filtered and concentrated. The residue was purified by silica gel flash chromatography (eluted with hexane/acetone (v/v 100:1)) to give the product **48**. During this process, we monitored the reaction using TLC and did not observe the formation of compound **1b**; the raw materials are basically not converted.

(1,2-diazidoethane-1,1-diyl)dibenzene (48)

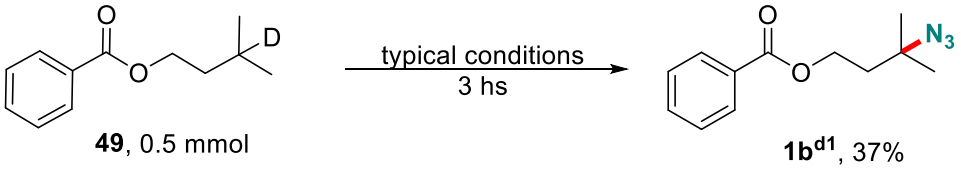


48

R_f = 0.5, 2% acetone in hexane, yellowish oil (90.0 mg, 34% yield)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 – 7.39 (m, 2H), 7.38 – 7.35 (m, 3H), 7.35 – 7.30 (m, 5H), 4.04 (s, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 140.28, 128.78, 128.47, 127.49, 72.58, 59.49.[5]

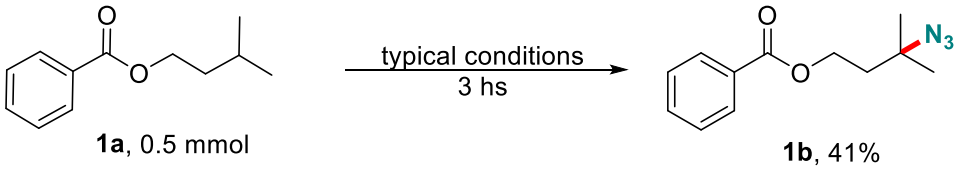
7.4 KIE experiments



49, 0.5 mmol

1b^{d1}, 37%

The 5 mL flat mouth test tube was equipped with two rubber plugs. A graphite felt (1 cm x 1.5 cm x 0.5 cm) and a nickel sheet (1 cm x 1 cm x 0.2 cm) are used as anode and cathode, respectively. The graphite felt anode is attached to a platinum wire. Substrate **49** (0.5 mmol, 1.0 equiv), K_3PO_4 (0.5 equiv), $Cu(acac)_2$ (5 mol%), NHPI (0.1 mmol, 20 mol%) were first dissolved in CH_3CN/H_2O (2.0 mL, 4/1) and stirred for 5 min at room temperature. Then the mixture was added with Bu_4NBF_4 (0.5 equiv). The reaction mixture was stirred and electrolyzed with a constant current of 10 mA at room temperature (23 °C) for 3 hours. Upon completion, the reaction mixture was extracted with DCM (3 x 2.0 mL). The combined organic solution was dried over anhydrous Na_2SO_4. Then the mixture was filtered and concentrated. The residue was purified by chromatography on silica gel to afford the desired product **1b** (43 mg, 37% yield).



1a, 0.5 mmol

1b, 41%

The 5 mL flat mouth test tube was equipped with two rubber plugs. A graphite felt (1 cm x 1.5 cm x 0.5 cm) and a nickel sheet (1 cm x 1 cm x 0.2 cm) are used as anode and cathode, respectively. The graphite felt anode is attached to a platinum wire. Substrate **49** (0.5 mmol, 1.0 equiv), K_3PO_4 (0.5 equiv), $Cu(acac)_2$ (5 mol%), NHPI (0.1 mmol, 20 mol%) were first dissolved in CH_3CN/H_2O (2.0 mL, 4/1) and stirred for 5 min at room temperature. Then the mixture was added with Bu_4NBF_4 (0.5 equiv). The reaction mixture was stirred and electrolyzed with a constant current of 10 mA at room temperature (23 ^oC) for 3 hours. Upon completion, the reaction mixture was extracted with DCM (3 x 2.0 mL). The combined organic solution was dried over anhydrous Na_2SO_4. Then the mixture was filtered and concentrated. The residue was purified by chromatography on silica gel to afford the desired product **1b** (47 mg, 41% yield).

7.5 Cyclic voltammetry (CV) experiments

The cyclic voltammograms were recorded in a mixed solvent of $MeCN/H_2O$ (2:4) with Bu_4NBF_4 (0.1 M) as supporting electrolyte using a glassy carbon disk working electrode (diameter, 1 mm), a Pt wire auxiliary electrode, and a SCE reference electrode. The scan rate was 50 mV/s unless other mentioned. Before the CV test, the solution is stirred for ten minutes.

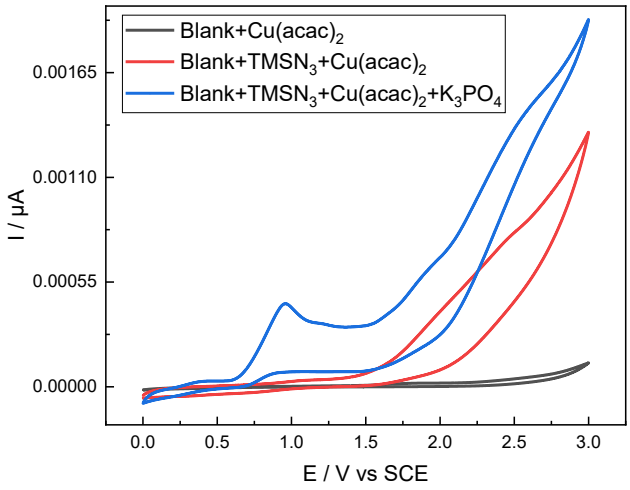


Figure 3. Cyclic voltammograms of copper species. $Cu(acac)_2$ (2.0 mM), $TMSN_3$ (10.0 mM), K_3PO_4 (5.0 mM).

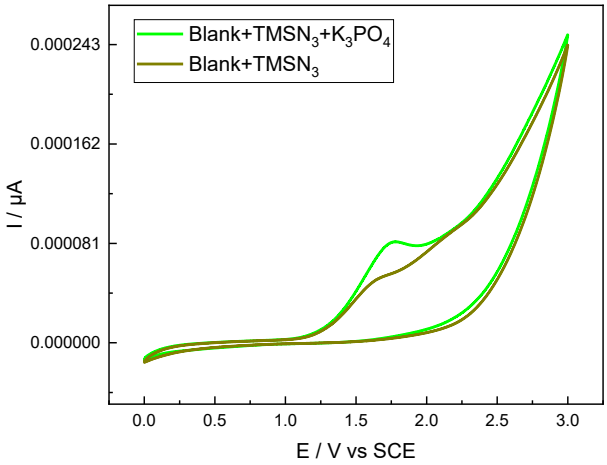


Figure 4. Cyclic voltammograms of azide species. $TMSN_3$ (10.0 mM), K_3PO_4 (5.0 mM).

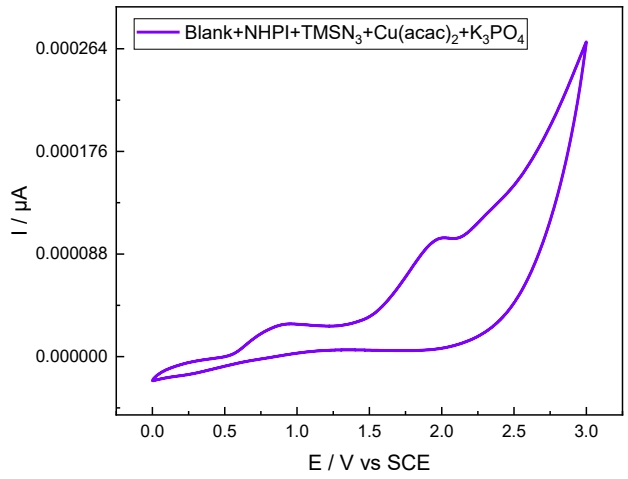


Figure 5. Cyclic voltammograms of NHPI With $TMSN_3$, $Cu(acac)_2$ and K_3PO_4. Note: NHPI (5 mM), $Cu(acac)_2$ (2.0 mM), $TMSN_3$ (10.0 mM), K_3PO_4 (5.0 mM).

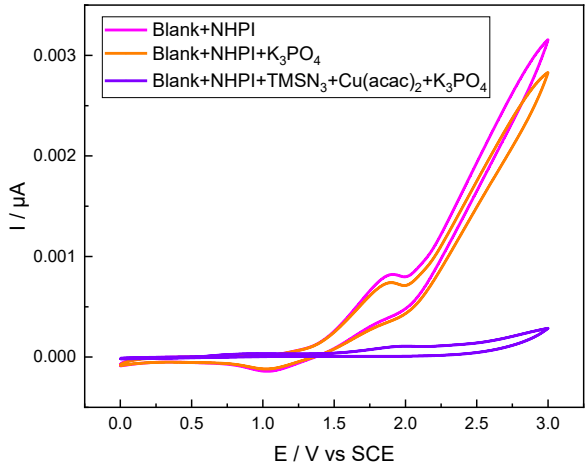


Figure 6. Cyclic voltammograms of NHPI species. NHPI (5 mM), $Cu(acac)_2$ (2.0 mM), $TMSN_3$ (10.0 mM), K_3PO_4 (5.0 mM).

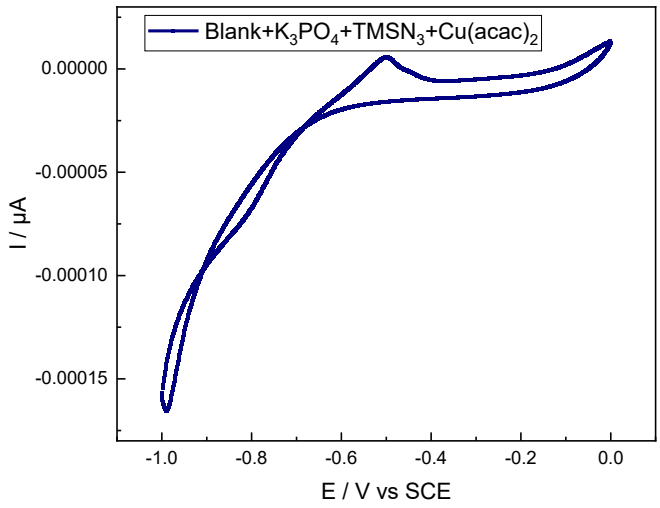
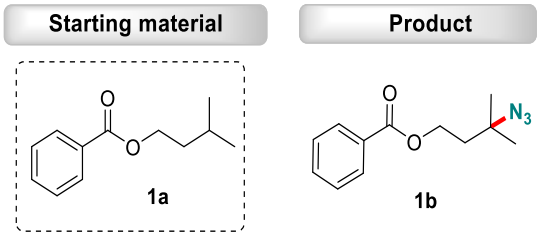


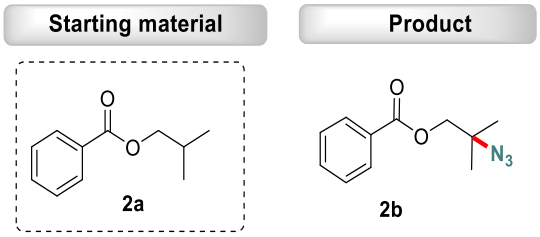
Figure 7. Cyclic voltammograms of copper azide species. $Cu(acac)_2$ (2.0 mM), $TMSN_3$ (10.0 mM), K_3PO_4 (5.0 mM).

8. Characterization data of products



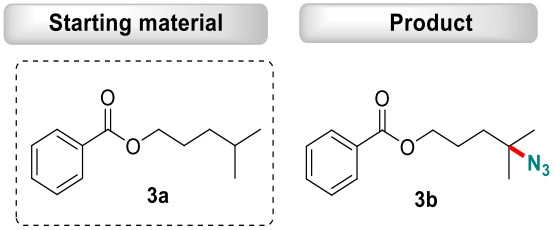
R_f = 0.6 (**1b**), 5% acetone in hexane

Compound **1b** (yellowish oil, 93 mg, 80% yield): **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.03 (d, J = 7.2 Hz, 2H), 7.55 (t, J = 7.4 Hz, 1H), 7.43 (t, J = 7.7 Hz, 2H), 4.43 (t, J = 6.8 Hz, 2H), 1.97 (t, J = 6.8 Hz, 2H), 1.37 (s, 6H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 166.52, 133.07, 130.19, 129.61, 128.46, 61.32, 60.33, 39.78, 26.44.[6]



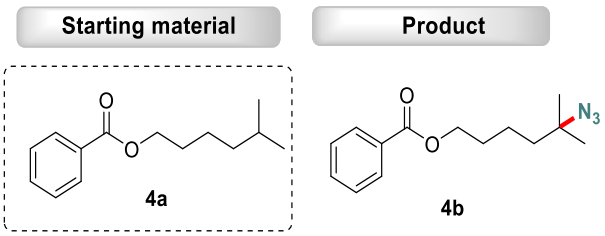
R_f = 0.6 (**2b**), 5% acetone in hexane

Compound **2b** (yellowish oil, 61 mg, 56% yield): **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.08 (d, J = 7.9 Hz, 2H), 7.59 (t, J = 7.4 Hz, 1H), 7.47 (t, J = 7.7 Hz, 2H), 4.25 (s, 2H), 1.39 (s, 6H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 166.26, 133.40, 129.90, 129.76, 128.64, 71.28, 60.35, 23.51. **HRMS (ESI-TOF) m/z:** $[M+H]^+$ Calcd for $C_{11}H_{14}N_3O_2$ 220.1081; Found: 220.1080.



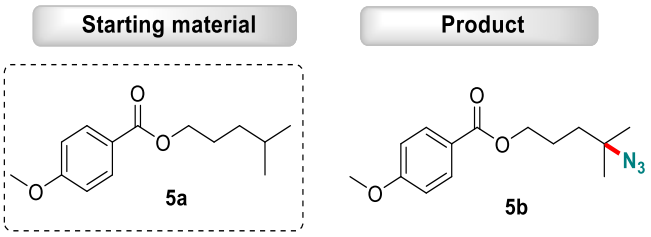
R_f = 0.6 (**3b**), 5% acetone in hexane

Compound **3b** (yellowish oil, 104 mg, 84% yield): **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.04 (d, J = 7.6 Hz, 2H), 7.56 (t, J = 7.4 Hz, 1H), 7.44 (t, J = 7.7 Hz, 2H), 4.33 (t, J = 6.5 Hz, 2H), 1.89 – 1.82 (m, 2H), 1.66 – 1.61 (m, 2H), 1.30 (s, 6H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 166.68, 133.05, 130.38, 129.67, 128.48, 64.97, 61.29, 37.96, 26.11, 23.96. **HRMS (ESI-TOF) m/z:** $[M+H]^+$ Calcd for $C_{13}H_{18}N_3O_2$ 248.1394; Found: 248.1390.



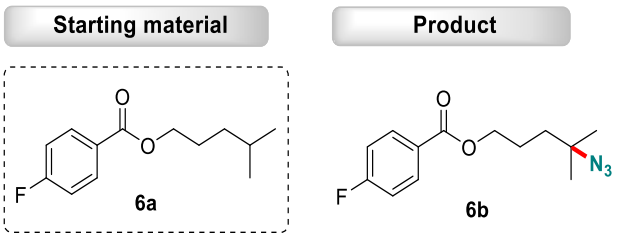
R_f = 0.6 (**4b**), 5% acetone in hexane

Compound **4b** (yellowish oil, 115 mg, 88% yield): **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.04 (d, J = 7.8 Hz, 2H), 7.55 (t, J = 7.4 Hz, 1H), 7.44 (t, J = 7.7 Hz, 2H), 4.33 (t, J = 6.6 Hz, 2H), 1.78 (p, J = 6.6 Hz, 2H), 1.61 – 1.49 (m, 4H), 1.27 (s, 6H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 166.69, 132.96, 130.47, 129.62, 128.44, 64.78, 61.56, 41.17, 29.05, 26.05, 20.94. **HRMS (ESI-TOF) m/z:** $[M+H]^+$ Calcd for $C_{14}H_{20}N_3O_2$ 262.1550; Found: 262.1549.



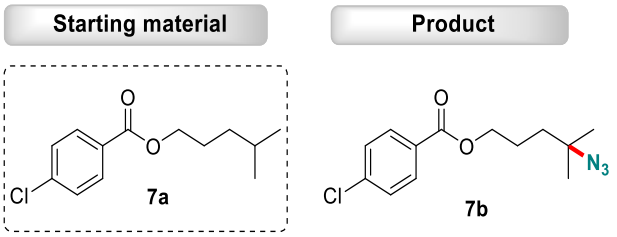
R_f = 0.5 (**5b**), 5% acetone in hexane

Compound **5b** (yellowish oil, 123 mg, 89% yield): **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.99 (d, J = 8.8 Hz, 2H), 6.91 (d, J = 8.8 Hz, 2H), 4.29 (t, J = 6.5 Hz, 2H), 3.85 (s, 3H), 1.83 (dt, J = 11.3, 6.6 Hz, 2H), 1.62 (dd, J = 10.5, 6.1 Hz, 2H), 1.29 (s, 6H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 166.41, 163.45, 131.66, 122.77, 113.70, 64.63, 61.30, 55.51, 37.93, 26.08, 23.98. **HRMS (ESI-TOF) m/z:** $[M+Na]^+$ Calcd for $C_{14}H_{19}N_3O_3Na$ 300.1319; Found: 300.1313.



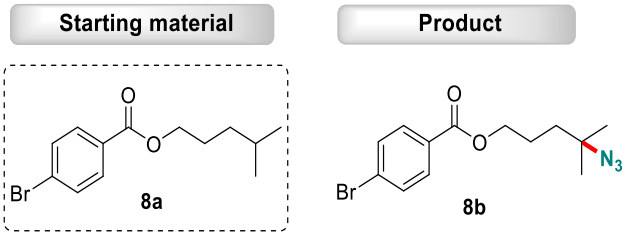
R_f = 0.5 (**6b**), 10% acetone in hexane

Compound **6b** (yellowish oil, 89 mg, 67% yield): **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.08 – 8.02 (m, 2H), 7.11 (t, J = 8.6 Hz, 2H), 4.32 (t, J = 6.5 Hz, 2H), 1.85 (dt, J = 11.5, 6.7 Hz, 2H), 1.62 (dd, J = 10.5, 6.1 Hz, 2H), 1.30 (s, 6H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 165.72, 132.18, 126.62, 115.73, 115.56, 65.11, 61.28, 37.94, 26.13, 23.95. **^{19}F NMR** (471 MHz, $CDCl_3$) δ -105.75. **HRMS (ESI-TOF) m/z:** $[M+H]^+$ Calcd for $C_{13}H_{17}FN_3O_2$ 266.1299; Found: 266.1292.



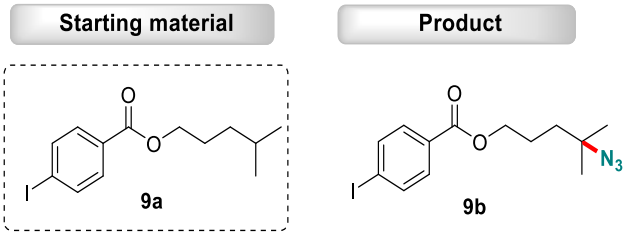
R_f = 0.5 (**7b**), 5% acetone in hexane

Compound **7b** (yellowish oil, 97 mg, 69% yield): **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.97 (d, J = 8.4 Hz, 2H), 7.41 (d, J = 8.4 Hz, 2H), 4.32 (t, J = 6.5 Hz, 2H), 1.84 (dt, J = 11.4, 6.7 Hz, 2H), 1.64 – 1.56 (m, 2H), 1.30 (s, 6H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 165.81, 139.51, 131.07, 128.84, 128.82, 65.21, 61.25, 37.90, 26.12, 23.91. **HRMS (ESI-TOF) m/z:** $[M+Na]^+$ Calcd for $C_{13}H_{16}ClN_3O_2Na$ 304.0823; Found: 304.0832.



R_f = 0.5 (**8b**), 5% acetone in hexane

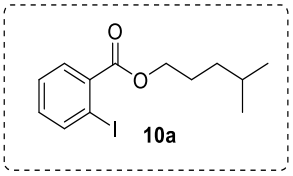
Compound **8b** (yellowish oil, 110 mg, 68% yield): **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.90 (d, J = 8.3 Hz, 2H), 7.58 (d, J = 8.3 Hz, 2H), 4.32 (t, J = 6.5 Hz, 2H), 1.85 (dd, J = 22.9, 6.7 Hz, 2H), 1.65 – 1.59 (m, 2H), 1.30 (s, 6H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 165.99, 131.88, 131.24, 129.30, 128.22, 65.27, 61.28, 37.93, 26.15, 23.93. **HRMS (ESI-TOF) m/z:** $[M+Na]^+$ Calcd for $C_{13}H_{16}BrN_3O_2Na$ 348.0318; Found: 348.0323.



R_f = 0.7 (**9b**), 10% acetone in hexane

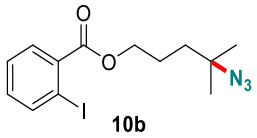
Compound **9b** (yellowish oil, 123 mg, 66% yield): **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.80 (d, J = 8.4 Hz, 2H), 7.74 (d, J = 8.3 Hz, 2H), 4.32 (t, J = 6.5 Hz, 2H), 1.87 – 1.81 (m, 2H), 1.63 – 1.59 (m, 2H), 1.30 (s, 6H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 166.18, 137.87, 131.13, 129.85, 100.86, 65.23, 61.26, 37.90, 26.14, 23.91. **HRMS (ESI-TOF) m/z:** $[M+H]^+$ Calcd for $C_{13}H_{17}IN_3O_2$ 374.0360; Found: 374.0363.

Starting material



10a

Product

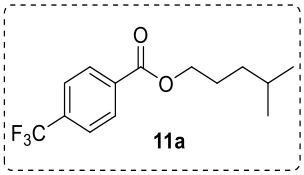


10b

R_f = 0.7 (**10b**), 10% acetone in hexane

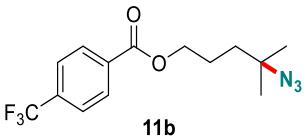
Compound **10b** (yellowish oil, 115 mg, 62% yield): **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.98 (d, J = 7.9 Hz, 1H), 7.78 (d, J = 7.7 Hz, 1H), 7.40 (t, J = 7.6 Hz, 1H), 7.14 (t, J = 7.4 Hz, 1H), 4.34 (t, J = 6.5 Hz, 2H), 1.86 (dd, J = 22.9, 6.6 Hz, 2H), 1.65 – 1.61 (m, 2H), 1.29 (s, 6H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 166.64, 141.37, 135.41, 132.69, 130.98, 128.01, 94.07, 65.71, 61.27, 38.05, 26.09, 23.79. **HRMS (ESI-TOF) m/z:** $[M+Na]^+$ Calcd for $C_{13}H_{16}IN_3O_2Na$ 396.0179; Found: 396.0173.

Starting material



11a

Product

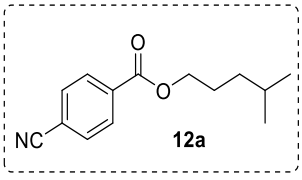


11b

R_f = 0.7 (**11b**), 10% acetone in hexane

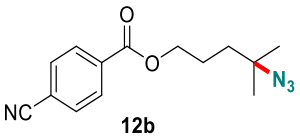
Compound **11b** (yellowish oil, 98 mg, 62% yield): **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.15 (d, J = 8.1 Hz, 2H), 7.71 (d, J = 8.2 Hz, 2H), 4.36 (t, J = 6.5 Hz, 2H), 1.90 – 1.84 (m, 2H), 1.64 – 1.61 (m, 2H), 1.31 (s, 6H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 165.47, 134.72, 133.61, 130.10, 125.57, 125.54, 65.55, 61.24, 37.90, 26.13, 23.90. **HRMS (ESI-TOF) m/z:** $[M+K]^+$ Calcd for $C_{14}H_{16}F_3N_3O_2K$ 354.0826; Found: 354.0833.

Starting material



12a

Product

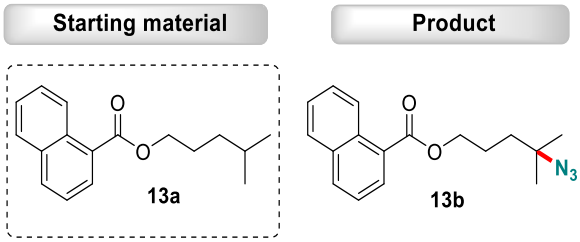


12b

R_f = 0.7 (**12b**), 10% acetone in hexane

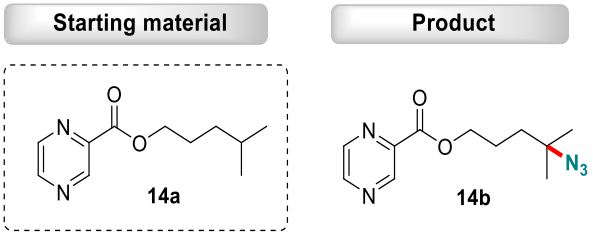
Compound **12b** (yellowish oil, 87 mg, 64% yield): **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.16 (d, J = 8.4 Hz, 2H), 7.77 (d, J = 8.4 Hz, 2H), 4.39 (t, J = 6.5 Hz, 2H), 1.90 (dd, J

= 15.3, 7.9 Hz, 2H), 1.66 – 1.62 (m, 2H), 1.33 (s, 6H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 165.04, 134.18, 132.37, 130.21, 118.09, 116.57, 65.81, 61.22, 37.87, 26.14, 23.86. **HRMS (ESI-TOF) m/z:** $[M+H]^+$ Calcd for $C_{14}H_{17}N_4O_2$ 273.1346; Found: 273.1346.



R_f = 0.6 (**13b**), 5% acetone in hexane

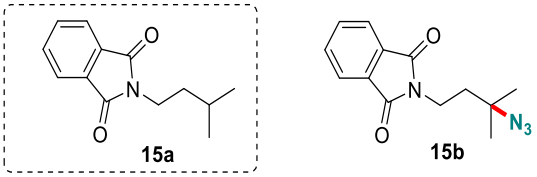
Compound **13b** (yellowish oil, 89 mg, 60% yield): **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.94 (d, J = 8.7 Hz, 1H), 8.20 (d, J = 7.2 Hz, 1H), 8.03 (d, J = 8.2 Hz, 1H), 7.89 (d, J = 8.2 Hz, 1H), 7.63 (t, J = 7.7 Hz, 1H), 7.53 (dt, J = 15.8, 7.8 Hz, 2H), 4.43 (t, J = 6.5 Hz, 2H), 1.97 – 1.87 (m, 2H), 1.72 – 1.64 (m, 2H), 1.32 (s, 6H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 167.61, 133.96, 133.47, 131.47, 130.24, 128.66, 127.85, 127.29, 126.31, 125.89, 124.60, 65.07, 61.29, 38.07, 26.10, 23.99. **HRMS (ESI-TOF) m/z:** $[M+H]^+$ Calcd for $C_{17}H_{20}N_3O_2$ 298.1550; Found: 298.1553.



R_f = 0.7 (**14b**), 10% acetone in hexane

Compound **14b** (yellowish oil, 81 mg, 65% yield): **^{1}H NMR** (500 MHz, $CDCl_3$) δ 9.31 (s, 1H), 8.81 – 8.72 (m, 2H), 4.45 (t, J = 6.7 Hz, 2H), 1.90 (dd, J = 15.9, 7.3 Hz, 2H), 1.61 (dd, J = 14.2, 6.0 Hz, 2H), 1.29 (s, 6H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 163.95, 147.76, 146.32, 144.61, 143.56, 66.34, 61.19, 37.76, 26.09, 23.86. **HRMS (ESI-TOF) m/z:** $[M+Na]^+$ Calcd for $C_{11}H_{15}N_5O_2Na$ 272.1118; Found: 272.1120.

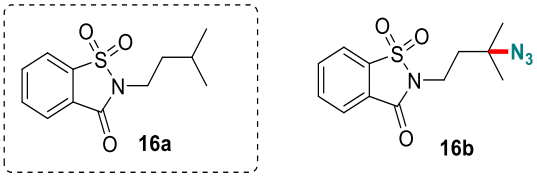
Starting material | Product



R_f = 0.5 (**15b**), 5% acetone in hexane

Compound **15b** (yellowish oil, 88 mg, 68% yield): **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.16 (d, J = 8.4 Hz, 2H), 7.77 (d, J = 8.4 Hz, 2H), 4.39 (t, J = 6.5 Hz, 2H), 1.90 (dd, J = 15.3, 7.9 Hz, 2H), 1.66 – 1.62 (m, 2H), 1.33 (s, 6H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 165.04, 134.18, 132.37, 130.21, 118.09, 116.57, 65.81, 61.22, 37.87, 26.14, 23.86.[7]

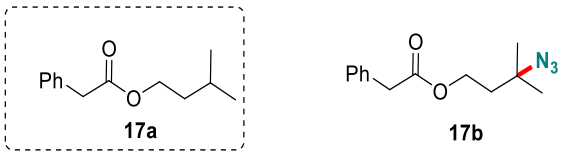
Starting material | Product



R_f = 0.5 (**16b**), 5% acetone in hexane

Compound **16b** (yellowish oil, 82 mg, 56% yield): **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.03 (d, J = 7.6 Hz, 1H), 7.90 (d, J = 7.4 Hz, 1H), 7.83 (dt, J = 19.1, 6.9 Hz, 2H), 3.88 – 3.82 (m, 2H), 2.03 – 1.96 (m, 2H), 1.37 (s, 6H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 158.70, 137.73, 134.84, 134.42, 127.38, 125.18, 121.00, 60.10, 39.31, 35.13, 25.94. **HRMS (ESI-TOF) m/z:** $[M+H]^+$ Calcd for $C_{12}H_{15}N_4O_3S$ 295.0859; Found: 295.0859.

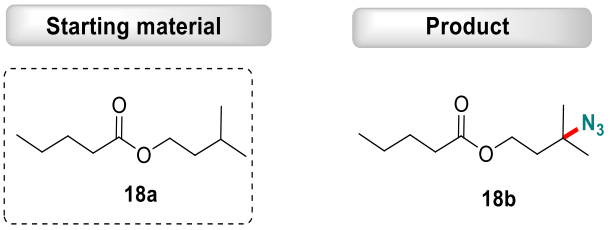
Starting material | Product



R_f = 0.6 (**17b**), 2% acetone in hexane

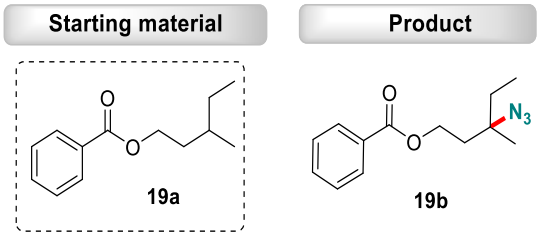
Compound **17b** (yellowish oil, 86 mg, 70% yield): **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.35 – 7.30 (m, 2H), 7.28 (d, J = 7.4 Hz, 2H), 4.20 (t, J = 6.8 Hz, 2H), 3.62 (s, 2H),

1.81 (t, J = 6.9 Hz, 2H), 1.27 (s, 6H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 171.56, 133.98, 129.37, 128.69, 127.24, 61.27, 60.27, 41.56, 39.67, 26.36.[7]



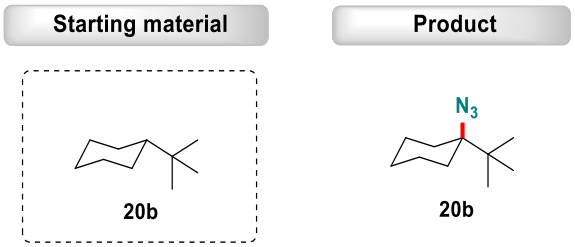
R_f = 0.5 (**18b**), 5% acetone in hexane

Compound **18b** (yellowish oil, 62 mg, 58% yield): **^{1}H NMR** (500 MHz, $CDCl_3$) δ 4.17 (t, J = 6.9 Hz, 2H), 2.29 (t, J = 7.6 Hz, 2H), 1.83 (t, J = 6.9 Hz, 2H), 1.59 (dd, J = 15.2, 7.6 Hz, 2H), 1.37 – 1.29 (m, 8H), 0.91 (t, J = 7.4 Hz, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 173.88, 60.62, 60.31, 39.78, 34.18, 27.11, 26.43, 22.38, 13.83. **HRMS (ESI-TOF) m/z:** $[M+H]^+$ Calcd for $C_{10}H_{20}N_3O_2$ 214.1550; Found: 214.1550.



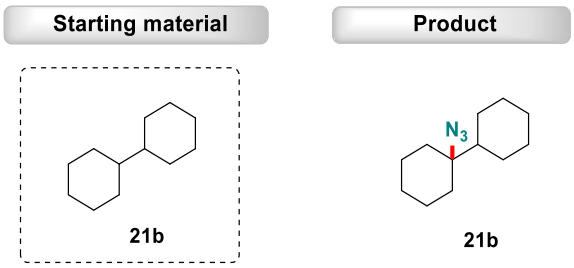
R_f = 0.6 (**19b**), 5% acetone in hexane

Compound **19b** (yellowish oil, 72 mg, 58% yield): **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.04 (d, J = 7.1 Hz, 2H), 7.56 (t, J = 7.4 Hz, 1H), 7.44 (t, J = 7.7 Hz, 2H), 4.58 (t, J = 6.9 Hz, 2H), 2.32 (dtd, J = 21.7, 14.5, 6.9 Hz, 2H), 1.95 (ddd, J = 38.5, 14.6, 7.3 Hz, 2H), 1.80 (s, 3H), 1.09 (t, J = 7.3 Hz, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 166.64, 133.14, 130.30, 129.71, 128.54, 70.66, 63.02, 43.24, 38.95, 31.45, 10.44.[7]



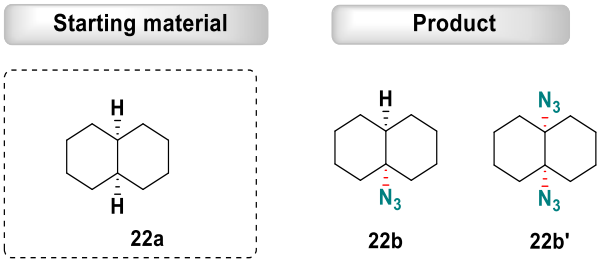
R_f = 0.6 (**20b**), hexane

Compound **20b** (yellowish oil, 70 mg, 77% yield): **^{1}H NMR** (500 MHz, $CDCl_3$) δ 1.80 (d, J = 12.7 Hz, 2H), 1.68 (dd, J = 27.1, 13.2 Hz, 3H), 1.45 (dt, J = 48.3, 13.3 Hz, 4H), 1.16 – 1.06 (m, 1H), 0.97 (s, 9H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 69.74, 40.63, 28.96, 25.82, 25.43, 22.70.[8]



R_f = 0.7 (**21b**), hexane

Compound **21b** (yellowish oil, 68 mg, 66% yield): ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.80 (d, J = 10.5 Hz, 4H), 1.66 (d, J = 12.5 Hz, 4H), 1.61 – 1.45 (m, 4H), 1.45 – 1.28 (m, 3H), 1.26 – 1.04 (m, 6H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 67.14, 47.74, 31.82, 27.28, 26.88, 26.58, 25.75, 22.35.[9]

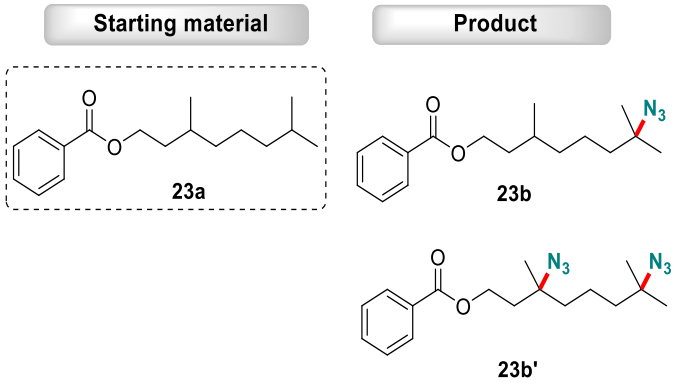


R_f = 0.6 (**22b**), R_f = 0.5 (**22b'**), hexane

Compound **22b** (yellowish oil, 42 mg, 47% yield): **^{1}H NMR** (500 MHz, CDCl3) δ 1.84 (d, J = 13.8 Hz, 2H), 1.78 – 1.69 (m, 2H), 1.60 (dd, J = 13.1, 10.3 Hz, 4H), 1.36 – 1.20 (m, 9H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 65.28, 44.52, 36.41, 28.84, 26.20, 22.15. **HRMS (ESI-TOF) m/z:** $[M+H]^+$ Calcd for $C_{10}H_{18}N_3$ 180.1495; Found: 180.1490.

Compound **22b'** (yellowish oil, 33 mg, 30% yield): **^{1}H NMR** (500 MHz, $CDCl_3$) δ 1.78 (d, J = 8.8 Hz, 2H), 1.61 (dd, J = 13.0, 5.7 Hz, 6H), 1.40 (d, J = 55.9 Hz, 8H).

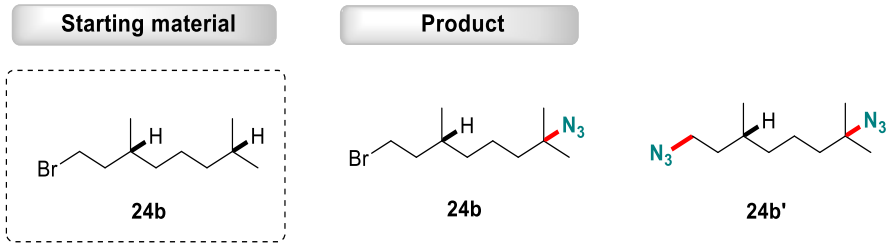
^{13}C NMR (126 MHz, $CDCl_3$) δ 65.04, 39.54, 27.96. **HRMS (ESI-TOF) m/z:** $[M+H]^+$ Calcd for $C_{10}H_{17}N_6$ 221.1509; Found: 221.1510.



R_f = 0.6 (**23b**), R_f = 0.5 (**23b'**), 1% acetone in hexane

Compound **23b** (yellowish oil, 65 mg, 43% yield): **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.04 (d, J = 7.7 Hz, 2H), 7.55 (t, J = 7.4 Hz, 1H), 7.44 (t, J = 7.7 Hz, 2H), 4.41 – 4.32 (m, 2H), 1.82 (td, J = 12.7, 7.0 Hz, 1H), 1.66 (dt, J = 11.9, 5.9 Hz, 1H), 1.59 – 1.55 (m, 1H), 1.40 (ddd, J = 23.9, 19.5, 8.5 Hz, 5H), 1.25 – 1.19 (m, 7H), 0.98 (d, J = 6.6 Hz, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 166.81, 132.97, 130.61, 129.67, 128.47, 63.57, 61.78, 41.79, 37.26, 35.68, 30.06, 26.13, 21.72, 19.65. **HRMS (ESI-TOF) m/z:** $[M+H]^+$ Calcd for $C_{17}H_{26}N_3O_2$ 304.2020; Found: 304.2021.

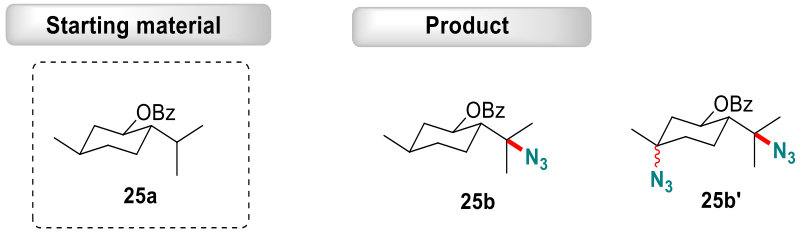
Compound **23b'** (yellowish oil, 64 mg, 37% yield): **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.04 (d, J = 7.5 Hz, 2H), 7.56 (t, J = 7.4 Hz, 1H), 7.44 (t, J = 7.7 Hz, 2H), 4.44 (t, J = 6.8 Hz, 2H), 2.04 – 1.95 (m, 2H), 1.58 (t, J = 6.9 Hz, 2H), 1.49 – 1.41 (m, 4H), 1.37 (s, 3H), 1.26 (s, 6H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 166.60, 133.17, 130.20, 129.69, 128.53, 62.89, 61.51, 61.19, 41.74, 40.16, 37.84, 26.08, 23.71, 18.91. **HRMS (ESI-TOF) m/z:** $[M+H]^+$ Calcd for $C_{17}H_{25}N_6O_2$ 345.2034; Found: 345.2025.



R_f = 0.6 (**24b**), R_f = 0.7 (**24b'**), hexane

Compound **24b** (yellowish oil, 102 mg, 78% yield): **^{1}H NMR** (500 MHz, $CDCl_3$) δ 3.49 – 3.35 (m, 2H), 1.87 (dd, J = 16.2, 8.0 Hz, 1H), 1.72 – 1.60 (m, 2H), 1.40 (ddd, J = 35.2, 20.1, 7.1 Hz, 5H), 1.24 (s, 6H), 1.14 (t, J = 12.4 Hz, 1H), 0.89 (d, J = 6.3 Hz, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 61.70, 41.69, 40.03, 36.76, 32.11, 31.59, 26.12, 26.08, 21.58, 18.93.[9]

Compound **24b'** (yellowish oil, 9 mg, 8% yield): **^{1}H NMR** (500 MHz, $CDCl_3$) δ 3.51 – 3.34 (m, 2H), 1.88 (dd, J = 16.2, 8.0 Hz, 1H), 1.68 (dd, J = 12.9, 5.7 Hz, 2H), 1.49 – 1.28 (m, 5H), 1.26 (s, 6H), 1.16 (dt, J = 13.7, 7.8 Hz, 1H), 0.90 (d, J = 6.2 Hz, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 61.78, 41.75, 40.07, 36.81, 32.19, 31.64, 26.19, 26.14, 21.64, 18.98. **HRMS (ESI-TOF) m/z:** $[M+K]^+$ Calcd for $C_{10}H_{20}N_6K$ 263.1381; Found: 263.1379.

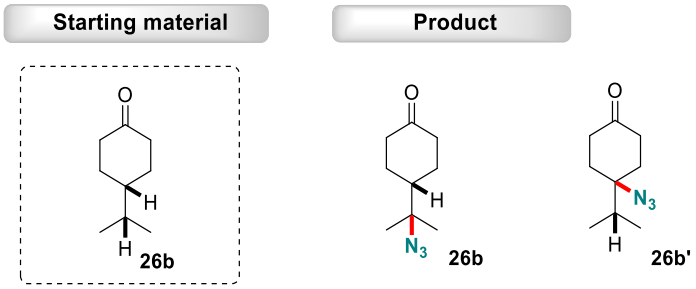


R_f = 0.7 (**25b**), R_f = 0.65 (**25b'**), 1% acetone in hexane

Compound **25b** (white solid, 80 mg, 53% yield): **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.05 (dd, J = 16.4, 7.6 Hz, 2H), 7.55 (t, J = 7.4 Hz, 1H), 7.44 (t, J = 7.7 Hz, 2H), 5.14 – 5.05 (m, 1H), 2.09 (d, J = 12.3 Hz, 1H), 2.00 (dd, J = 16.9, 3.4 Hz, 1H), 1.84 (dd, J = 18.5, 7.9 Hz, 1H), 1.80 – 1.72 (m, 1H), 1.62 – 1.55 (m, 1H), 1.41 – 1.08 (m, 9H), 0.93 (d, J = 6.6 Hz, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 165.78, 133.01, 130.73, 129.72, 128.49, 73.96, 63.68, 49.26, 41.44, 34.19, 31.33, 26.66, 25.26, 24.61, 21.83.[7]

Compound **25b'** (white solid, 13 mg, 8% yield): **^{1}H NMR** (500 MHz, CDCl3) δ 8.05 (d, J = 7.2 Hz, 2H), 7.57 (t, J = 7.4 Hz, 1H), 7.45 (t, J = 7.7 Hz, 2H), 5.34 (dd, J = 10.6, 4.4 Hz, 1H), 2.21 (dd, J = 13.3, 7.2 Hz, 1H), 1.93 – 1.82 (m, 3H), 1.58 – 1.38 (m, 4H), 1.37 (s, 3H), 1.31 (d, J = 5.6 Hz, 6H). **^{13}C NMR** (126 MHz, CDCl3) δ 165.48,

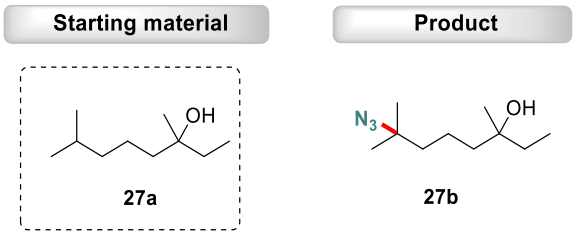
133.22, 130.35, 129.77, 128.57, 70.87, 63.57, 62.02, 48.86, 42.61, 35.95, 26.54, 25.28, 24.42, 22.63.[7]



R_f = 0.6 (**26b**), R_f = 0.7 (**26b'**), 5% acetone in hexane

Compound **26b** (yellowish oil, 65 mg, 72% yield): **^{1}H NMR** (500 MHz, $CDCl_3$) δ 2.37 (d, J = 14.8 Hz, 2H), 2.28 (td, J = 14.3, 5.9 Hz, 2H), 2.08 (dd, J = 11.7, 4.3 Hz, 2H), 1.79 – 1.70 (m, 1H), 1.53 – 1.43 (m, 2H), 1.26 (s, 6H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 210.99, 63.65, 45.71, 40.60, 27.24, 23.67.[8]

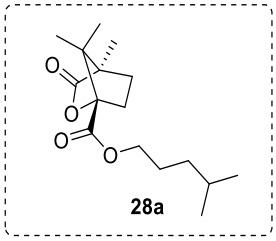
Compound **26b'** (yellowish oil, 6 mg, 7% yield): **^{1}H NMR** (500 MHz, $CDCl_3$) δ 2.59 (td, J = 14.3, 6.1 Hz, 2H), 2.31 (d, J = 15.1 Hz, 2H), 2.01 (ddd, J = 29.2, 13.9, 6.5 Hz, 3H), 1.85 (t, J = 13.6 Hz, 2H), 1.03 (d, J = 6.8 Hz, 6H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 210.44, 65.70, 37.25, 36.63, 31.36, 17.70.[8]



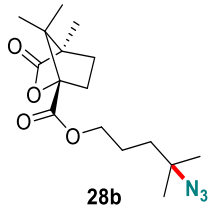
R_f = 0.4 (**27b**), 10% acetone in hexane

Compound **27b** (yellowish oil, 70 mg, 71% yield): **^{1}H NMR** (500 MHz, $CDCl_3$) δ 1.48 (dt, J = 11.2, 5.3 Hz, 4H), 1.44 – 1.34 (m, 4H), 1.26 (d, J = 5.2 Hz, 6H), 1.16 (d, J = 5.2 Hz, 3H), 0.90 (dt, J = 12.7, 6.4 Hz, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 72.93, 61.80, 42.13 41.58, 34.51, 26.48, 26.12, 18.74, 8.33. **HRMS (ESI-TOF) m/z:** $[M+Na]^+$ Calcd for $C_{10}H_{21}N_3ONa$ 222.1577; Found: 222.1574.

Starting material



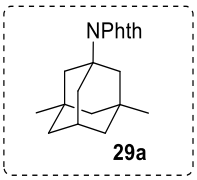
Product



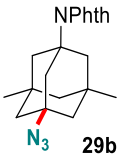
R_f = 0.5 (**28b**), 5% acetone in hexane

Compound **28b** (yellowish oil, 137 mg, 85% yield): **^{1}H NMR** (500 MHz, $CDCl_3$) δ 4.23 (dd, J = 11.3, 4.6 Hz, 2H), 2.42 (dd, J = 19.3, 9.2 Hz, 1H), 2.02 (t, J = 13.7 Hz, 1H), 1.95 – 1.87 (m, 1H), 1.76 (dd, J = 23.0, 6.7 Hz, 2H), 1.68 (dd, J = 10.9, 6.9 Hz, 1H), 1.53 (dd, J = 10.4, 6.2 Hz, 2H), 1.27 (s, 6H), 1.10 (s, 3H), 1.05 (s, 3H), 0.95 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 178.23, 167.59, 91.21, 65.61, 61.14, 54.89, 54.24, 37.79, 30.79, 29.06, 26.06, 23.79, 16.90, 16.87, 9.81. **HRMS (ESI-TOF) m/z:** $[M+H]^+$ Calcd for $C_{16}H_{26}N_3O_4$ 324.1918; Found: 324.1911.

Starting material



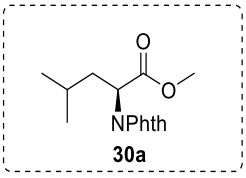
Product



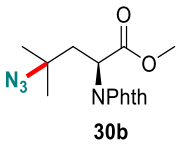
R_f = 0.5 (**29b**), 5% acetone in hexane

Compound **29b** (white solid, 136 mg, 78% yield): **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.75 (d, J = 8.3 Hz, 2H), 7.71 – 7.65 (m, 2H), 2.44 (s, 2H), 2.12 (d, J = 5.8 Hz, 4H), 1.55 (d, J = 11.5 Hz, 2H), 1.43 (d, J = 11.7 Hz, 2H), 1.25 (d, J = 12.7 Hz, 1H), 1.16 (d, J = 12.7 Hz, 1H), 0.98 (s, 6H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 169.56, 134.01, 131.83, 122.83, 61.85, 60.76, 49.15, 46.53, 44.95, 42.74, 33.98, 29.51.[9]

Starting material

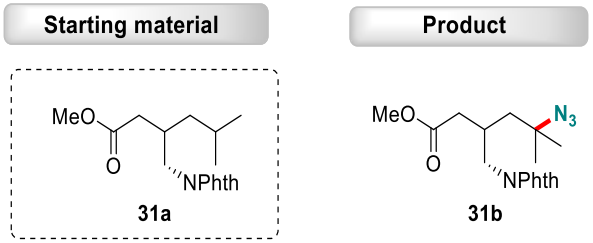


Product



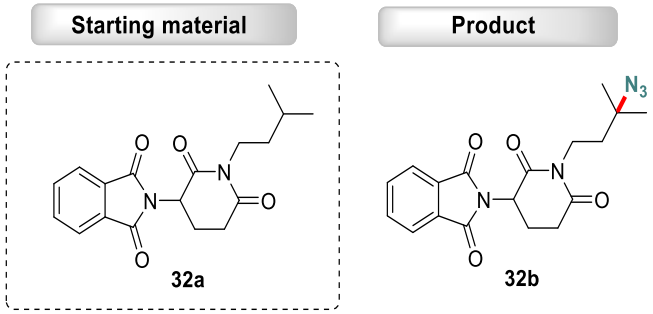
R_f = 0.6 (**30b**), 20% acetone in hexane

Compound **30b** (yellowish oil, 104 mg, 66% yield): **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.87 (d, J = 8.4 Hz, 2H), 7.76 – 7.72 (m, 2H), 5.05 (d, J = 12.8 Hz, 1H), 3.72 (s, 3H), 2.52 (dd, J = 15.3, 10.2 Hz, 1H), 2.45 – 2.39 (m, 1H), 1.36 (s, 3H), 1.30 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 169.82, 167.69, 134.35, 131.98, 123.71, 60.31, 53.20, 48.63, 39.06, 26.87, 25.36.[10]



R_f = 0.5 (**31b**), 10% acetone in hexane

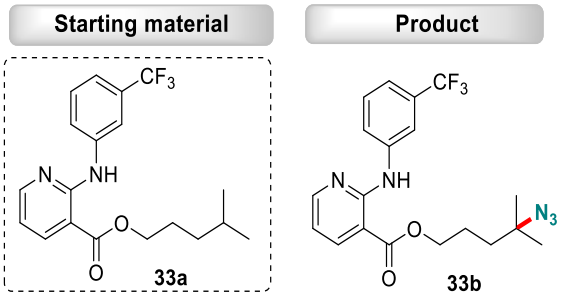
Compound **31b** (yellowish oil, 120 mg, 70% yield): **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.87 – 7.81 (m, 2H), 7.74 – 7.69 (m, 2H), 3.84 (dd, J = 13.8, 5.5 Hz, 1H), 3.64 (dd, J = 13.8, 8.5 Hz, 1H), 3.58 (s, 3H), 2.54 (dt, J = 12.0, 6.0 Hz, 1H), 2.45 – 2.34 (m, 2H), 1.56 (d, J = 5.3 Hz, 2H), 1.36 (s, 3H), 1.32 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 172.64, 168.73, 134.18, 132.07, 123.43, 61.28, 51.70, 43.26, 42.53, 38.06, 31.46, 26.44, 26.36.[7]



R_f = 0.6 (**32b**), 5% acetone in hexane

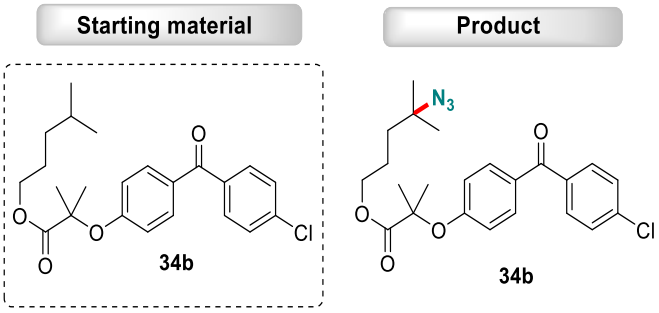
Compound **32b** (white solid, 122 mg, 66% yield): **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.90 – 7.81 (m, 2H), 7.78 – 7.70 (m, 2H), 4.97 (dd, J = 7.5, 5.1 Hz, 1H), 3.96 – 3.80 (m, 2H), 3.01 – 2.89 (m, 1H), 2.83 – 2.71 (m, 2H), 2.16 – 2.06 (m, 1H), 1.75 – 1.63 (m, 2H), 1.28 (s, 3H), 1.28 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 170.75, 168.48,

167.47, 134.51, 131.80, 123.79, 60.42, 50.18, 38.49, 36.74, 32.04, 25.94, 25.92, 22.02. **HRMS (ESI-TOF) m/z:** $[M+H]^+$ Calcd for $C_{18}H_{20}N_5O_4$ 370.1510; Found: 370.1507.



R_f = 0.5 (**33b**), 20% acetone in hexane

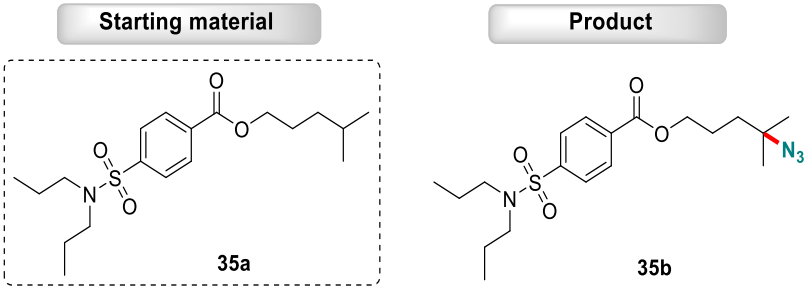
Compound **33b** (yellowish oil, 118 mg, 58% yield): **^{1}H NMR** (500 MHz, $CDCl_3$) δ 10.38 (s, 1H), 8.42 (d, J = 6.7 Hz, 1H), 8.26 (d, J = 9.8 Hz, 1H), 8.09 (s, 1H), 7.88 (d, J = 8.2 Hz, 1H), 7.43 (t, J = 8.0 Hz, 1H), 7.28 (d, J = 7.7 Hz, 1H), 6.83 – 6.76 (m, 1H), 4.35 (t, J = 6.5 Hz, 2H), 1.88 (dd, J = 23.0, 6.6 Hz, 2H), 1.67 – 1.61 (m, 2H), 1.32 (s, 6H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 167.58, 155.95, 153.24, 140.48, 140.29, 131.16, 129.33, 123.63, 119.14, 117.25, 114.22, 107.61, 65.46, 61.25, 37.96, 29.85, 26.16, 23.88. **^{19}F NMR** (471 MHz, $CDCl_3$) δ -62.63. **HRMS (ESI-TOF) m/z:** $[M+H]^+$ Calcd for $C_{19}H_{21}N_5O_2F_3$ 408.1642; Found: 408.1645.



R_f = 0.5 (**34b**), 5% acetone in hexane

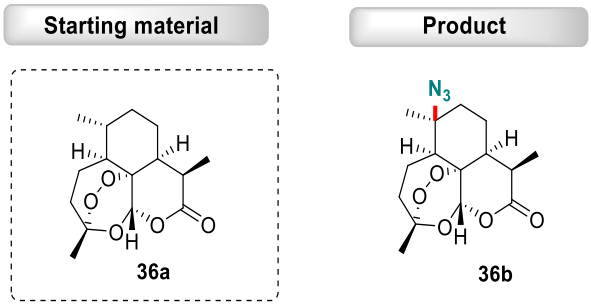
Compound **34b** (yellowish oil, 179 mg, 81% yield): **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.73 (d, J = 8.7 Hz, 2H), 7.69 (d, J = 8.4 Hz, 2H), 7.43 (d, J = 8.4 Hz, 2H), 6.85 (d, J = 8.7 Hz, 2H), 4.15 (t, J = 6.4 Hz, 2H), 1.69 – 1.59 (m, 8H), 1.33 (dd, J = 9.9, 6.6 Hz, 2H), 1.17 (s, 6H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 194.17, 173.76, 159.80, 138.47,

136.44, 132.14, 131.22, 130.43, 128.65, 117.21, 79.50, 65.69, 61.02, 37.66, 25.97, 25.56, 23.58. **HRMS (ESI-TOF) m/z:** $[M+H]^+$ Calcd for $C_{23}H_{27}N_3O_4Cl$ 444.1685; Found: 444.1687.



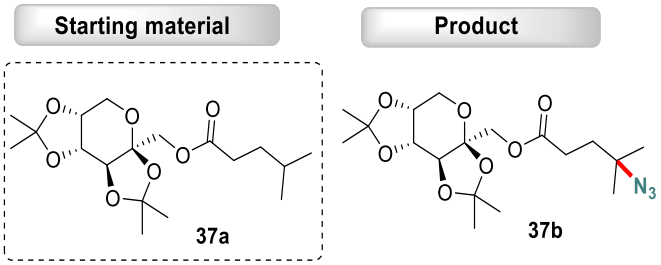
R_f = 0.5 (**35b**), 20% acetone in hexane

Compound **35b** (yellowish oil, 141 mg, 69% yield): **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.15 (d, J = 8.2 Hz, 2H), 7.88 (d, J = 8.2 Hz, 2H), 4.36 (t, J = 6.5 Hz, 2H), 3.16 – 3.03 (m, 4H), 1.90 – 1.81 (m, 2H), 1.67 – 1.61 (m, 2H), 1.57 – 1.51 (m, 4H), 1.31 (s, 6H), 0.87 (t, J = 7.4 Hz, 6H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 165.38, 144.46, 133.66, 130.34, 127.17, 65.66, 61.26, 50.09, 37.92, 26.16, 23.91, 22.09, 11.31. **HRMS (ESI-TOF) m/z:** $[M+K]^+$ Calcd for $C_{19}H_{30}N_4O_4SK$ 449.1619; Found: 449.1615.



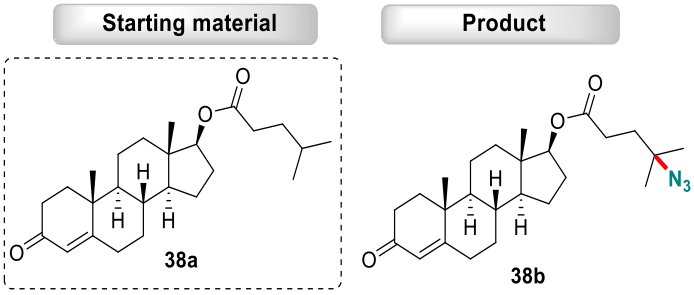
R_f = 0.4 (**36b**), 10% acetone in hexane

Compound **36b** (white solid, 76 mg, 47% yield): **^{1}H NMR** (500 MHz, $CDCl_3$) δ 6.40 (s, 1H), 3.38 – 3.30 (m, 1H), 2.46 – 2.36 (m, 1H), 2.14 – 2.09 (m, 1H), 2.04 – 1.95 (m, 2H), 1.84 – 1.76 (m, 3H), 1.69 (dd, J = 11.7, 6.8 Hz, 1H), 1.45 – 1.38 (m, 7H), 1.22 (d, J = 7.3 Hz, 4H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 172.01, 105.36, 93.87, 79.35, 64.08, 51.88, 45.26, 37.21, 35.53, 32.87, 25.33, 25.07, 19.93, 19.88, 12.69.[10]



R_f = 0.6 (**37b**), 5% acetone in hexane

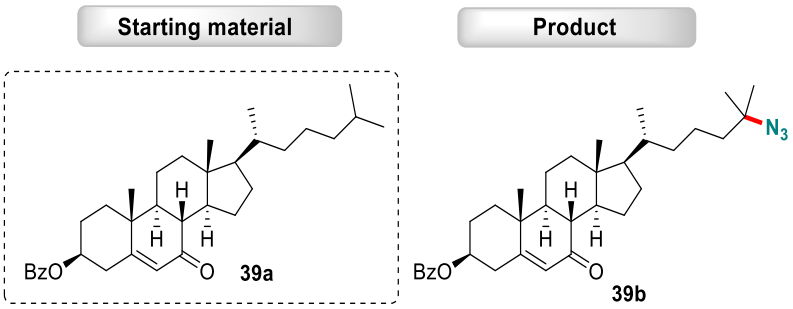
Compound **37b** (yellowish oil, 121 mg, 61% yield): **^{1}H NMR** (500 MHz, $CDCl_3$) δ 4.61 (d, J = 10.3 Hz, 1H), 4.41 (d, J = 11.7 Hz, 1H), 4.30 (d, J = 2.5 Hz, 1H), 4.24 (d, J = 7.9 Hz, 1H), 4.05 (d, J = 11.7 Hz, 1H), 3.91 (d, J = 13.0 Hz, 1H), 3.77 (d, J = 13.0 Hz, 1H), 2.49 – 2.41 (m, 2H), 1.88 – 1.81 (m, 2H), 1.55 (s, 3H), 1.48 (s, 3H), 1.41 (s, 3H), 1.34 (s, 3H), 1.28 (s, 6H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 172.66, 109.30, 108.90, 101.64, 70.91, 70.73, 70.20, 65.67, 61.40, 60.81, 36.20, 29.40, 26.62, 26.03, 25.99, 25.38, 24.21. **HRMS (ESI-TOF) m/z:** $[M+H]^+$ Calcd for $C_{18}H_{30}N_3O_7$ 400.2078; Found: 400.2075.



R_f = 0.5 (**38b**), 5% acetone in hexane

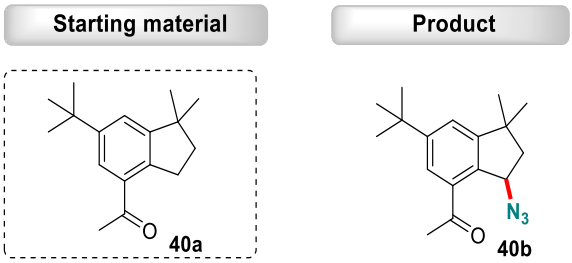
Compound **38b** (white solid, 134 mg, 63% yield): **^{1}H NMR** (500 MHz, $CDCl_3$) δ 5.73 (s, 1H), 4.61 (t, J = 8.5 Hz, 1H), 2.38 (dt, J = 14.4, 5.8 Hz, 4H), 2.28 (d, J = 13.9 Hz, 1H), 2.21 – 2.15 (m, 1H), 2.02 (dd, J = 17.1, 3.9 Hz, 1H), 1.81 (dd, J = 19.6, 12.3 Hz, 3H), 1.74 – 1.65 (m, 2H), 1.57 – 1.49 (m, 2H), 1.43 – 1.35 (m, 2H), 1.27 (d, J = 18.1 Hz, 8H), 1.20 – 1.15 (m, 4H), 1.04 (dd, J = 21.2, 7.1 Hz, 2H), 0.98 – 0.87 (m, 2H), 0.84 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 199.59, 173.37, 171.06, 124.10, 82.76, 60.96, 53.84, 50.38, 42.67, 38.76, 36.77, 36.39, 35.85, 35.55, 34.07, 32.88, 31.63,

29.78, 27.61, 26.00, 23.62, 20.68, 17.55, 12.23. **HRMS (ESI-TOF) m/z:** $[M+H]^+$ Calcd for $C_{25}H_{37}N_3O_3$ 466.2467; Found: 466.2467.



R_f = 0.5 (**39b**), 5% acetone in hexane

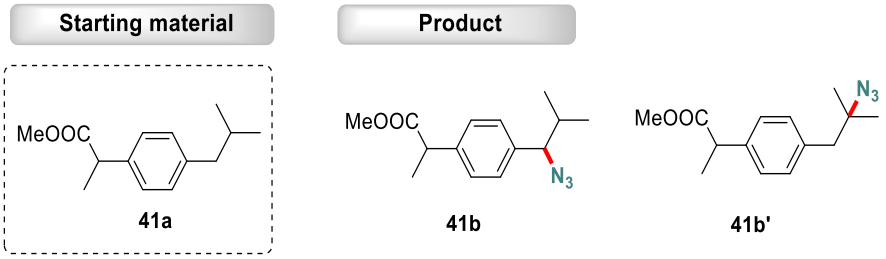
Compound **39b** (white solid, 161 mg, 61% yield): **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.04 (d, J = 7.7 Hz, 2H), 7.56 (t, J = 7.4 Hz, 1H), 7.44 (t, J = 7.7 Hz, 2H), 5.75 (s, 1H), 4.98 (td, J = 11.3, 5.5 Hz, 1H), 2.74 – 2.58 (m, 2H), 2.42 (dd, J = 17.1, 9.4 Hz, 1H), 2.26 (t, J = 10.9 Hz, 1H), 2.13 (d, J = 12.3 Hz, 1H), 2.03 (t, J = 12.7 Hz, 2H), 1.86 (dt, J = 24.3, 10.4 Hz, 2H), 1.57 (dd, J = 20.9, 9.1 Hz, 4H), 1.46 – 1.33 (m, 6H), 1.29 – 1.23 (m, 10H), 1.22 – 1.14 (m, 2H), 1.14 – 1.03 (m, 2H), 0.97 – 0.84 (m, 5H), 0.70 (s, 2H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 202.06, 165.91, 164.01, 133.16, 130.40, 129.71, 128.49, 126.92, 72.92, 61.90, 54.85, 50.08, 49.94, 45.56, 43.28, 42.03, 38.80, 38.52, 38.00, 36.31, 36.18, 35.78, 28.70, 27.61, 26.43, 26.19, 26.16, 21.32, 20.92, 18.93, 17.46, 12.13. **HRMS (ESI-TOF) m/z:** $[M+Na]^+$ Calcd for $C_{34}H_{47}NaN_3O_3$ 568.3510; Found: 568.3505.



R_f = 0.7 (**40b**), 5% acetone in hexane

Compound **40b** (yellowish oil, 113 mg, 79% yield): **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.75 (s, 1H), 7.40 (s, 1H), 5.59 (d, J = 7.0 Hz, 1H), 2.65 (s, 3H), 2.19 (dd, J = 13.7, 7.4 Hz, 1H), 2.08 (d, J = 13.6 Hz, 1H), 1.38 – 1.31 (m, 15H). **^{13}C NMR** (126 MHz,

$CDCl_3$) δ 199.95, 154.88, 153.39, 136.30, 134.07, 125.95, 124.09, 63.40, 48.05, 42.88, 35.14, 31.54, 30.81, 29.38, 28.27.[9]



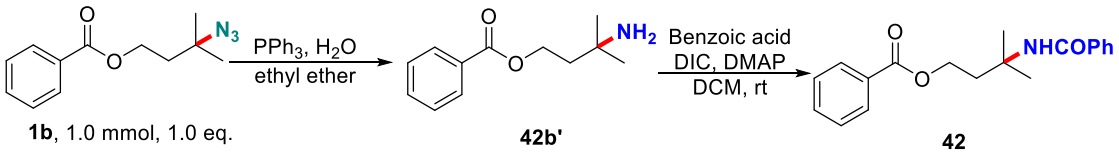
R_f = 0.7 (**41b**), R_f = 0.6 (**41b**), 1% acetone in hexane

Compound **41b** (yellowish oil, 60 mg, 46% yield): **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.29 (d, J = 7.9 Hz, 2H), 7.21 (d, J = 8.0 Hz, 2H), 4.12 (d, J = 7.9 Hz, 1H), 3.73 (q, J = 7.1 Hz, 1H), 3.67 (s, 3H), 1.97 (dq, J = 13.7, 6.8 Hz, 1H), 1.50 (d, J = 7.2 Hz, 3H), 1.01 (d, J = 6.6 Hz, 3H), 0.79 (d, J = 6.7 Hz, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 175.02, 140.32, 138.02, 127.78, 127.75, 73.00, 52.21, 45.23, 34.15, 19.67, 19.25, 18.69.[9]

Compound **41b'** (yellowish oil, 18 mg, 14% yield): **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.24 (d, J = 7.9 Hz, 2H), 7.16 (d, J = 7.9 Hz, 2H), 3.72 (q, J = 7.1 Hz, 1H), 3.66 (s, 3H), 2.74 (s, 2H), 1.50 (d, J = 7.2 Hz, 3H), 1.26 (s, 6H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 175.15, 139.06, 135.78, 130.85, 127.31, 61.94, 52.15, 47.18, 45.16, 26.02, 18.70.[9]

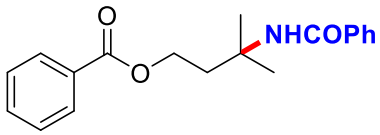
9. Conversion of organic azides

9.1 Converted to compound 42



To a solution of **1b** (233 mg, 1.0 mmol) in ethyl ether (2.5 mL) at 0 °C, PPh_3 (1.0 mmol) was added and allowed to stir for 1.5 h. Water (0.2 mL) was then added to the reaction mixture and allowed to stir for another 24 hs. The reaction mixture was poured over 10% aqueous HCl, extracted with ethyl ether (3 x 2 mL). The aqueous layer was made basic (pH 9.0) with 10% aqueous NaOH and extracted with ethyl ether (5 x 1 mL). Subsequently, the organic layer was spin-dried to obtain the crude

product **42b'**. Dissolve the crude product **42b'** in 4 ml of DCM, and then benzoic acid (1.0 mmol, 1.0 equiv.), 4-dimethylamino pyridine (0.1 equiv.), and *N,N'*-diisopropylcarbodiimide (DIC) (1.0 mmol, 1.0 equiv.) were added to a flask. The reaction mixture was allowed to stir at room temperature overnight before being quenched with H_2O (3.0 mL), and the mixture was extracted with CH_2Cl_2 (3 x 4.0 mL). The combined organic layer was dried over anhydrous Na_2SO_4, filtered, and concentrated in *vacuo*. The crude residue was purified by flash column chromatography on silica gel to afford the target compound **42** (230 mg, 74% yield).

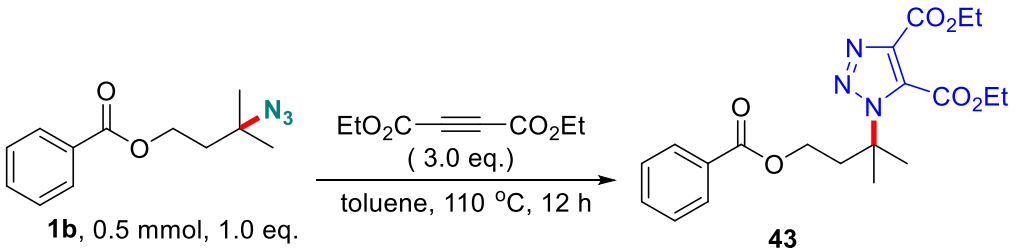


42

R_f = 0.5, 10% acetone in hexane, white solid (230 mg, 74% yield)

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.98 (d, J = 7.2 Hz, 2H), 7.71 (d, J = 7.2 Hz, 2H), 7.53 (t, J = 7.4 Hz, 1H), 7.45 (t, J = 7.4 Hz, 1H), 7.37 (dd, J = 16.3, 8.0 Hz, 4H), 6.21 (s, 1H), 4.47 (t, J = 6.5 Hz, 2H), 2.37 (t, J = 6.5 Hz, 2H), 1.59 (s, 3H), 1.55 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 167.19, 166.84, 135.60, 133.10, 131.35, 130.21, 129.68, 128.61, 128.59 , 126.88, 62.08, 53.41, 38.58, 27.62. **HRMS (ESI-TOF) m/z:** $[M+H]^+$ Calcd for $C_{19}H_{22}NO_3$ 312.1594; Found: 312.1591.

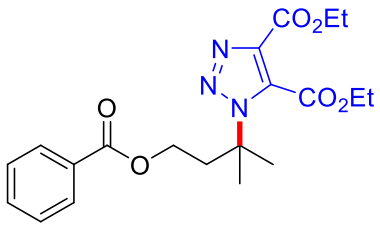
9.2 Converted to compound 43



1b, 0.5 mmol, 1.0 eq. **43**

In a heat gun-dried Schlenk tube equipped with a teflon-coated stirring bar, **1b** (116 mg, 0.5 mmol, 1 equiv.) was dissolved in toluene (4.0 mL). Diethyl acetylenedicarboxylate (3.0 equiv.) was added, and the resulting solution was heated at 110 °C for 12 h. After completion, the reaction mixture was cooled down to room

temperature and concentrated under reduced pressure. The crude reaction mixture was purified by flash column chromatography through silica gel (eluent: petroleum ether/ethyl acetate = 10:1) afforded the triazole compound **43** (175 mg, 87%) as a yellowish oil.

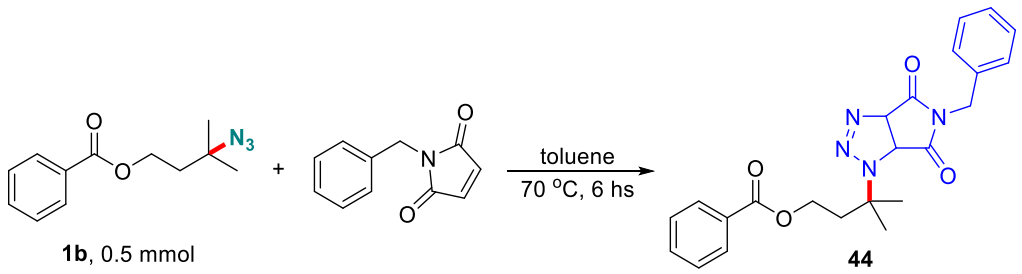


43

R_f = 0.3, 20% acetone in hexane, yellowish oil (175 mg, 87% yield)

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.83 (d, J = 7.1 Hz, 2H), 7.49 (t, J = 7.4 Hz, 1H), 7.35 (t, J = 7.7 Hz, 2H), 4.40 (q, J = 7.2 Hz, 2H), 4.30 (q, J = 7.1 Hz, 4H), 2.50 (t, J = 6.2 Hz, 2H), 1.78 (s, 6H), 1.37 – 1.28 (m, 6H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 166.19, 161.42, 159.85, 138.56, 132.98, 132.87, 129.82, 129.50, 128.33, 64.79, 63.52, 61.46, 60.51, 40.57, 27.89, 14.21, 13.74. **HRMS (ESI-TOF) m/z:** $[M+H]^+$ Calcd for $C_{20}H_{26}N_3O_6$ 404.1816; Found: 404.1823.

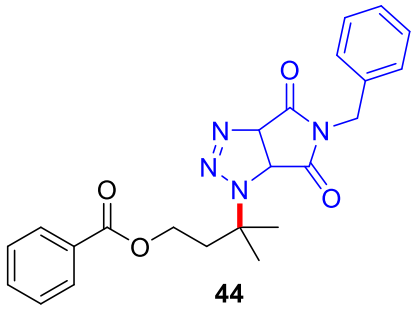
9.3 Converted to compound 44



1b, 0.5 mmol

44

To a flask containing *N*-benzylmaleimide (0.5 mmol, 1.0 equiv.) was added **1b** (116 mg, 0.5 mmol). The resulting clear solution was stirred at 70 °C for 24 h. After completion, the reaction mixture was cooled down to room temperature and concentrated under reduced pressure. The crude mixture was purified by flash column chromatography through silica gel (eluent: petroleum ether/ethyl acetate = 10:1) afforded the tetrazole **44** (147 mg, 70 %) as a white solid.

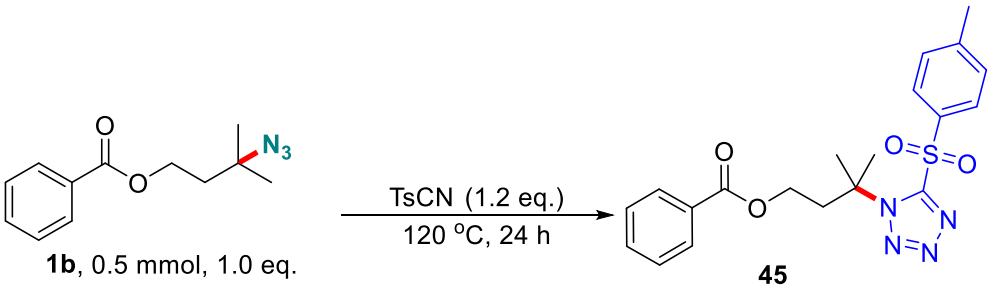


44

R_f = 0.3, 20% acetone in hexane, white solid (147 mg, 70% yield)

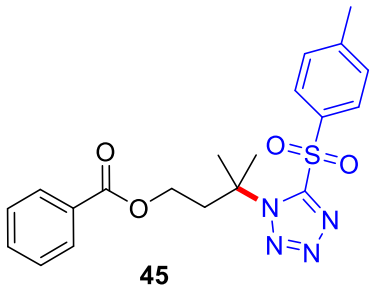
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.97 (d, J = 8.2 Hz, 2H), 7.54 (t, J = 7.4 Hz, 1H), 7.42 (t, J = 7.7 Hz, 2H), 7.32 – 7.20 (m, 5H), 5.43 (d, J = 11.0 Hz, 1H), 4.57 – 4.44 (m, 3H), 4.40 – 4.27 (m, 2H), 2.43 – 2.19 (m, 2H), 1.53 (d, J = 18.1 Hz, 6H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 172.60, 170.05, 166.40, 134.74, 133.06, 130.03, 129.48, 128.73, 128.65, 128.45, 128.23, 81.68, 61.13, 60.09, 56.74, 42.79, 39.63, 27.21, 27.18. **HRMS (ESI-TOF) m/z:** $[M+H]^+$ Calcd for $C_{23}H_{25}N_4O_4$ 421.1870; Found: 421.1873.

9.4 Converted to compound 45



1b, 0.5 mmol, 1.0 eq. **45**

In a heat gun-dried Schlenk tube equipped with a teflon-coated stirring bar, **1b** (116 mg, 0.5 mmol, 1 equiv.) and tosyl cyanide (TsCN, 1.2 equiv.) were mixed and heated at 120 °C for 24 h. After completion, the reaction mixture was cooled down to room temperature and concentrated under reduced pressure. The crude mixture was purified by flash column chromatography through silica gel (eluent: petroleum ether/ethyl acetate = 1:4) afforded the tetrazole **45** (195 mg, 94 %) as a white solid.

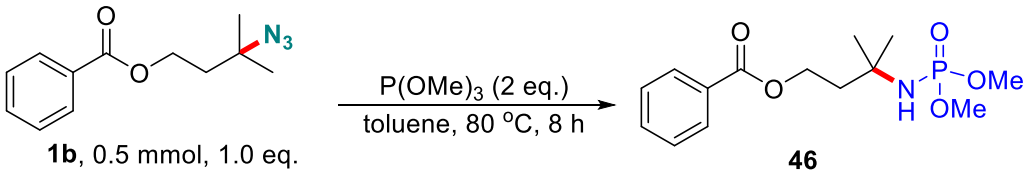


45

R_f = 0.4, 20% hexane in acetone, white solid (195 mg, 94% yield)

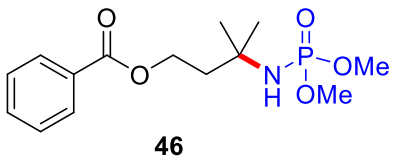
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.90 – 7.75 (m, 4H), 7.53 (t, J = 7.3 Hz, 1H), 7.38 (dd, J = 13.4, 7.9 Hz, 4H), 4.40 (t, J = 6.1 Hz, 2H), 2.74 (t, J = 6.1 Hz, 2H), 2.48 (s, 3H), 2.04 (s, 6H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 166.24, 156.28, 147.15, 134.94, 133.17, 130.63, 130.05, 129.63, 128.48, 127.76, 66.68, 60.53, 40.04, 28.50, 22.02. **HRMS (ESI-TOF) m/z:** $[M+H]^+$ Calcd for $C_{20}H_{23}N_4O_4S$ 415.1435; Found: 415.1439.

9.5 Converted to compound 46



1b, 0.5 mmol, 1.0 eq. **46**

In a heat gun-dried Schlenk tube equipped with a teflon-coated stirring bar, **1b** (116 mg, 0.5 mmol, 1.0 equiv.) was dissolved in toluene (3.0 mL). Trimethyl phosphite (2 equiv.) was added, and the resulting solution was heated at 80 °C for 8 h. After completion, the reaction mixture was cooled down to room temperature and concentrated under reduced pressure. The crude reaction mixture was purified by flash column chromatography using silica gel (eluent: petroleum ether/ethyl acetate = 10:1) to afford product **46** (142 mg, 90 %) as a white solid.

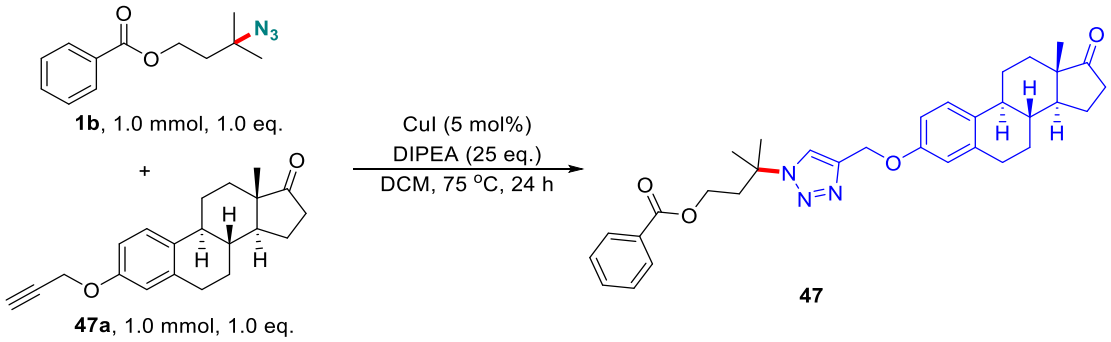


46

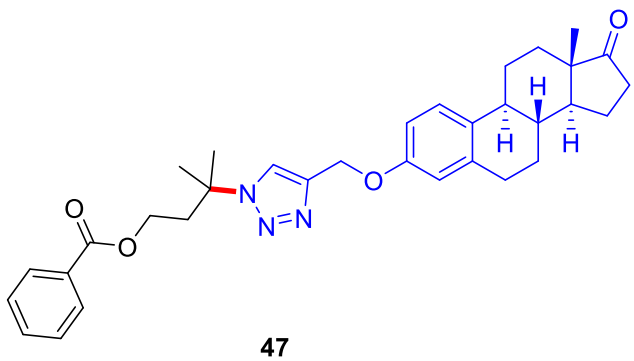
R_f = 0.4, 10% EtOAc in hexane, white solid (142 mg, 90% yield)

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.98 (d, J = 7.2 Hz, 2H), 7.51 (t, J = 7.4 Hz, 1H), 7.39 (t, J = 7.7 Hz, 2H), 4.43 (t, J = 6.7 Hz, 2H), 3.67 (d, J = 11.2 Hz, 6H), 3.01 (s, 1H), 1.98 (t, J = 6.6 Hz, 2H), 1.30 (s, 6H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 166.57, 132.99, 130.23, 129.54, 128.42, 61.84, 53.03, 52.20, 41.89, 29.16. **HRMS (ESI-TOF) m/z:** $[M+H]^+$ Calcd for $C_{14}H_{23}NO_5P$ 316.1308; Found: 316.1303.

9.6 Converted to compound 47



A suspension of **1b** (233 mg, 1.0 mmol, 1.0 equiv.), CuI (5 mol%), DIPEA (25 equiv.), and **47a** (1.0 equiv.) were heated through a heating block at 75 °C in CH_2Cl_2 (2 mL) for 24 h. After completion, the reaction mixture was cooled down to room temperature and concentrated under reduced pressure. The crude reaction mixture was purified by flash column chromatography using silica gel (eluent: petroleum ether/ethyl acetate = 5:1) to afford product **47** (444 mg, 82 %) as a white solid. It is worth noting that the transformation of raw materials is poorer when the temperature is lower during the reaction process.



R_f = 0.4, 30% EtOAc in hexane, white solid (444 mg, 82% yield)

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.92 (d, J = 7.9 Hz, 2H), 7.70 (s, 1H), 7.54 (t, J = 7.4 Hz, 1H), 7.41 (t, J = 7.7 Hz, 2H), 7.19 (d, J = 8.6 Hz, 1H), 6.82 – 6.75 (m, 1H), 6.72 (s, 1H), 5.09 (s, 2H), 4.27 (t, J = 6.5 Hz, 2H), 2.88 (dd, J = 10.6, 4.6 Hz, 2H), 2.55 – 2.44 (m, 3H), 2.37 (d, J = 11.4 Hz, 1H), 2.22 (dd, J = 13.5, 6.9 Hz, 1H), 2.18 – 2.08 (m, 1H), 2.07 – 1.98 (m, 2H), 1.98 – 1.86 (m, 2H), 1.77 (s, 6H), 1.60 (d, J = 12.0 Hz, 1H), 1.51 – 1.34 (m, 4H), 0.89 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 220.91, 166.35, 156.47, 144.01, 137.92, 133.14, 132.69, 129.90, 129.60, 128.45, 126.45, 120.36, 114.90, 112.43, 62.34, 60.90, 60.80, 50.49, 48.06, 44.05, 41.06, 38.39, 35.93, 31.66, 29.70, 28.29, 26.59, 25.96, 21.65, 13.93. **HRMS (ESI-TOF) m/z:** $[M+H]^+$ Calcd for $C_{33}H_{40}N_3O_4$ 542.3013; Found: 542.3011.

10. References

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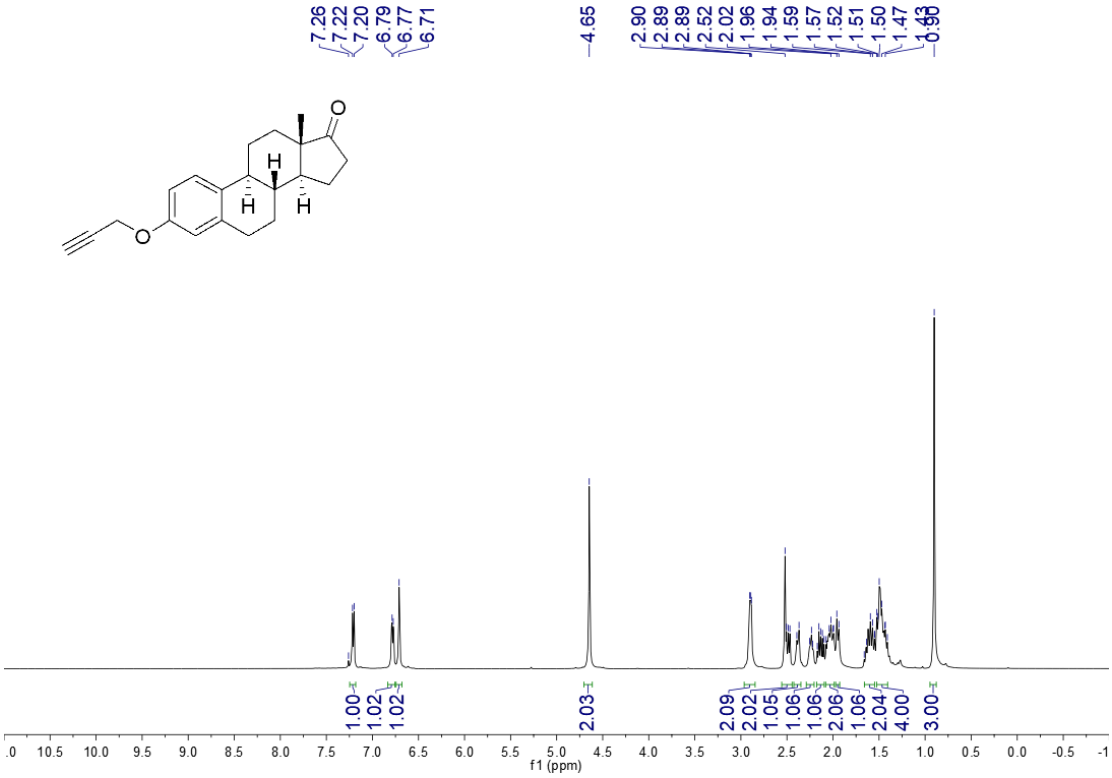
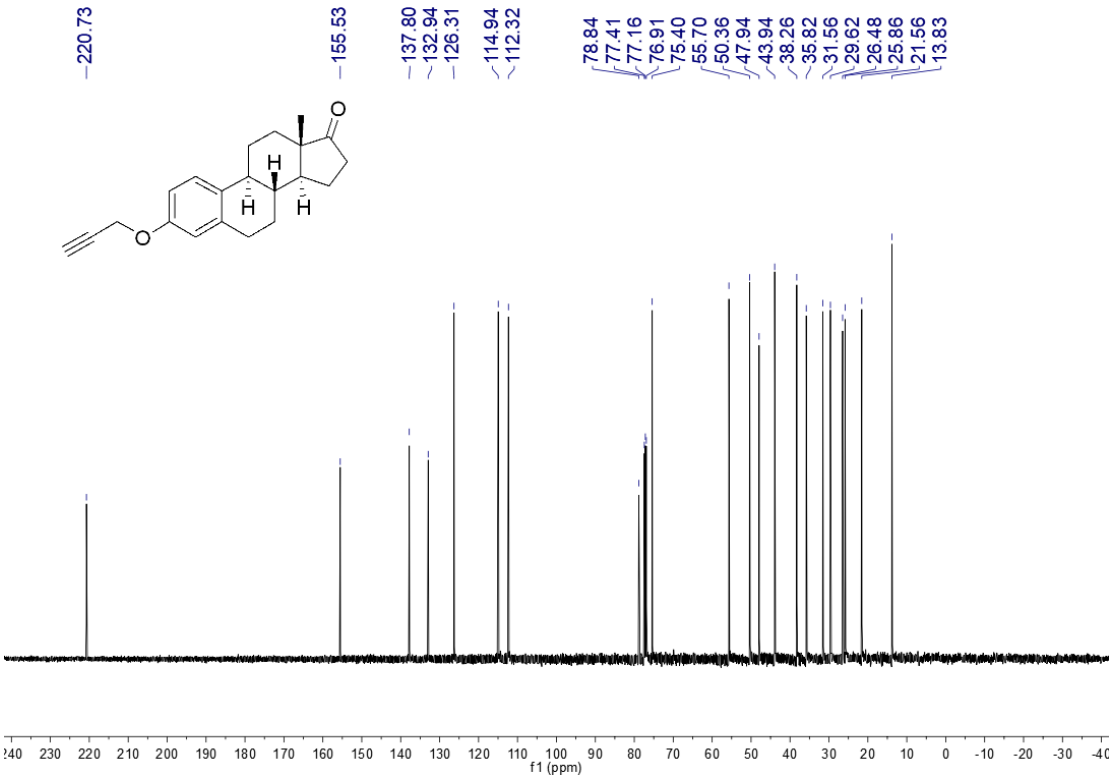
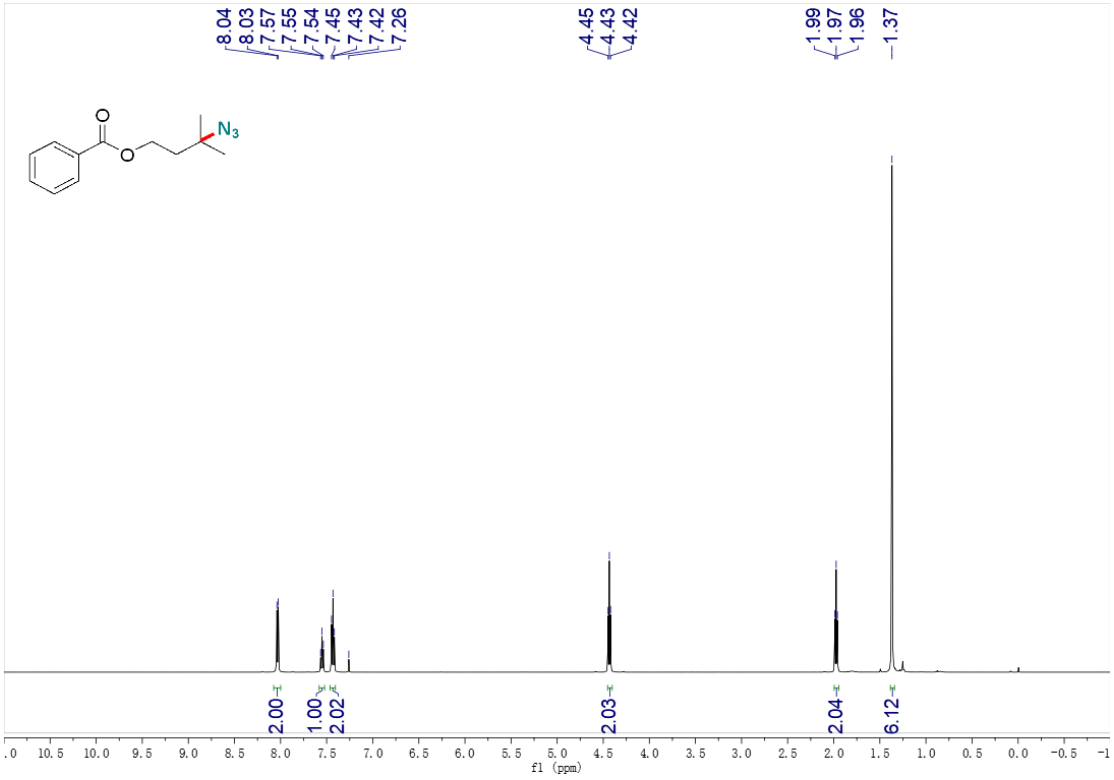
11. ^{1}H-NMR and ^{13}C-NMR spectra



^{1}H NMR of compound **47a** (500 MHz, $CDCl_3$)



^{13}C NMR of compound **47a** (126 MHz, $CDCl_3$)



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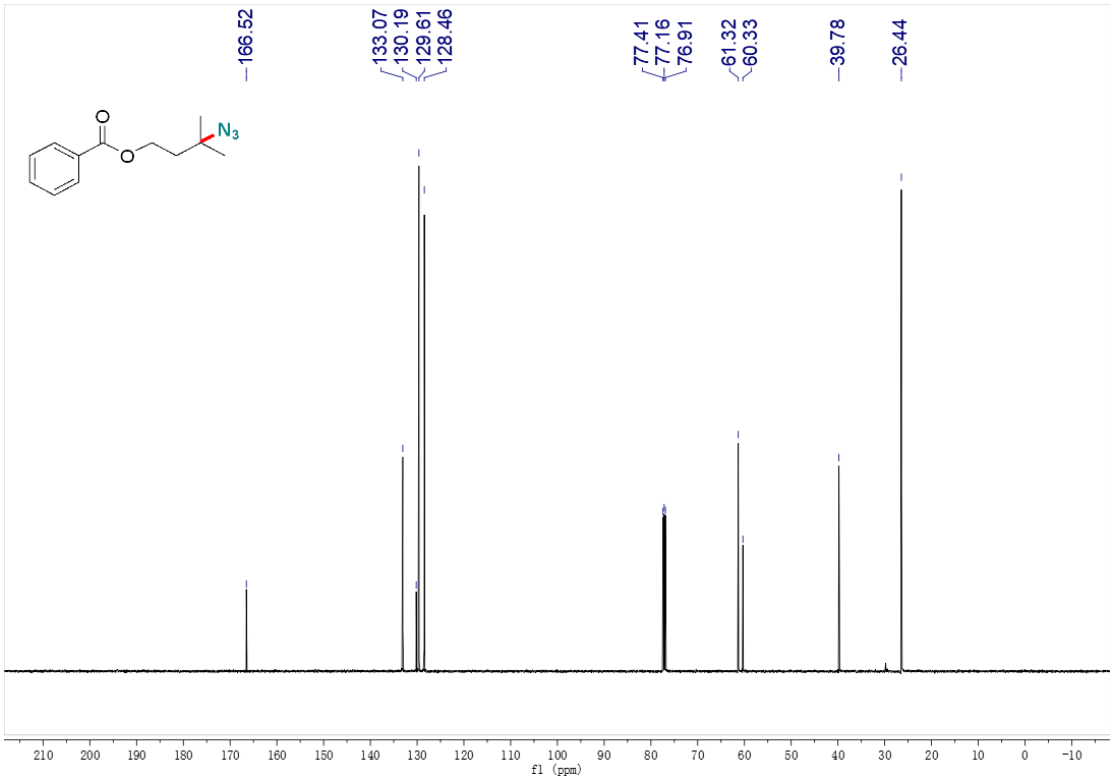
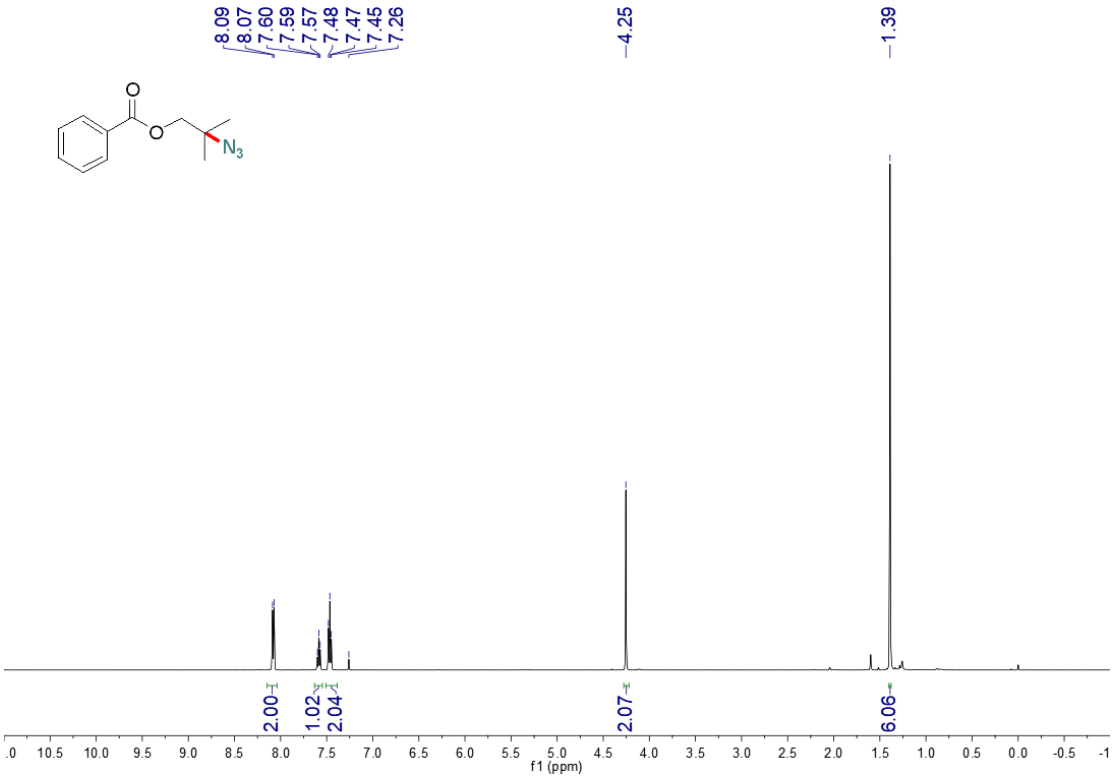
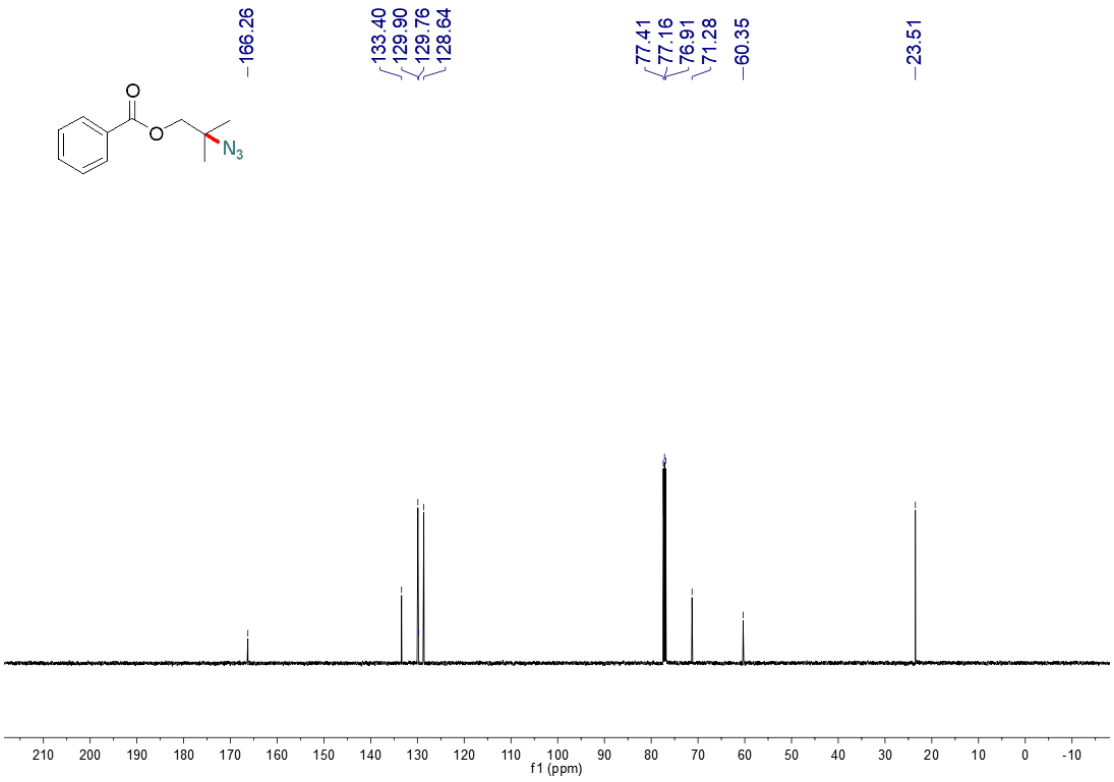


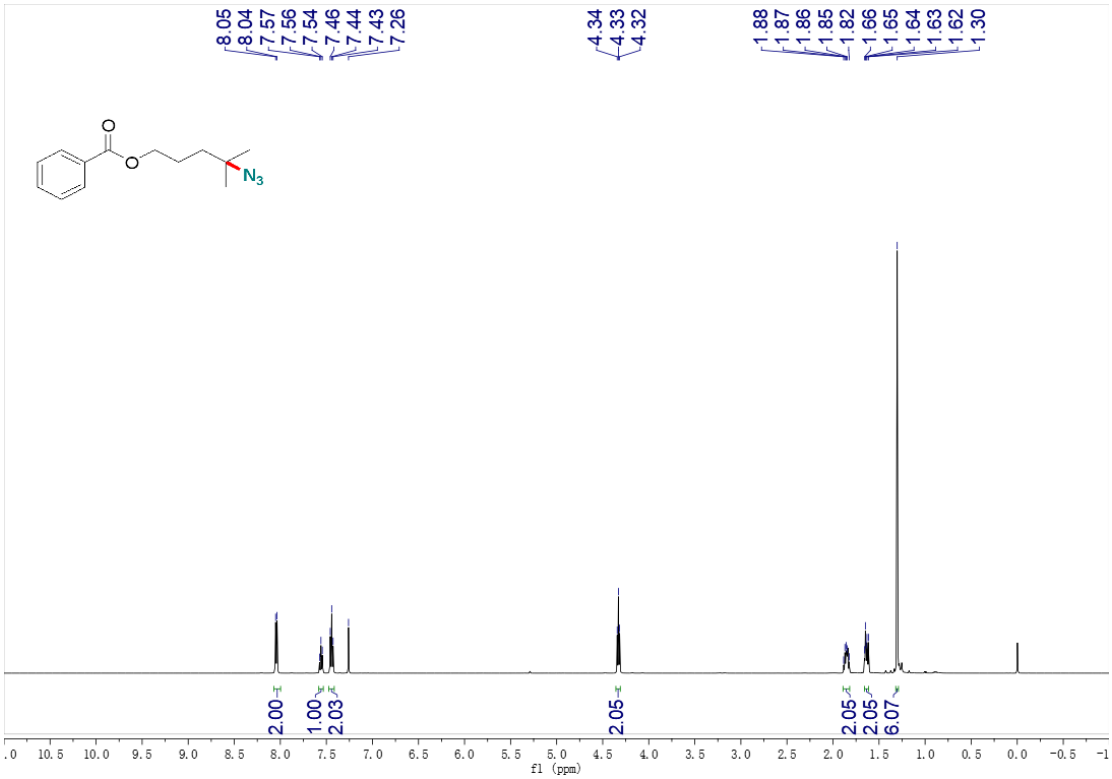
^{13}C NMR of compound **1b** (126 MHz, $CDCl_3$)



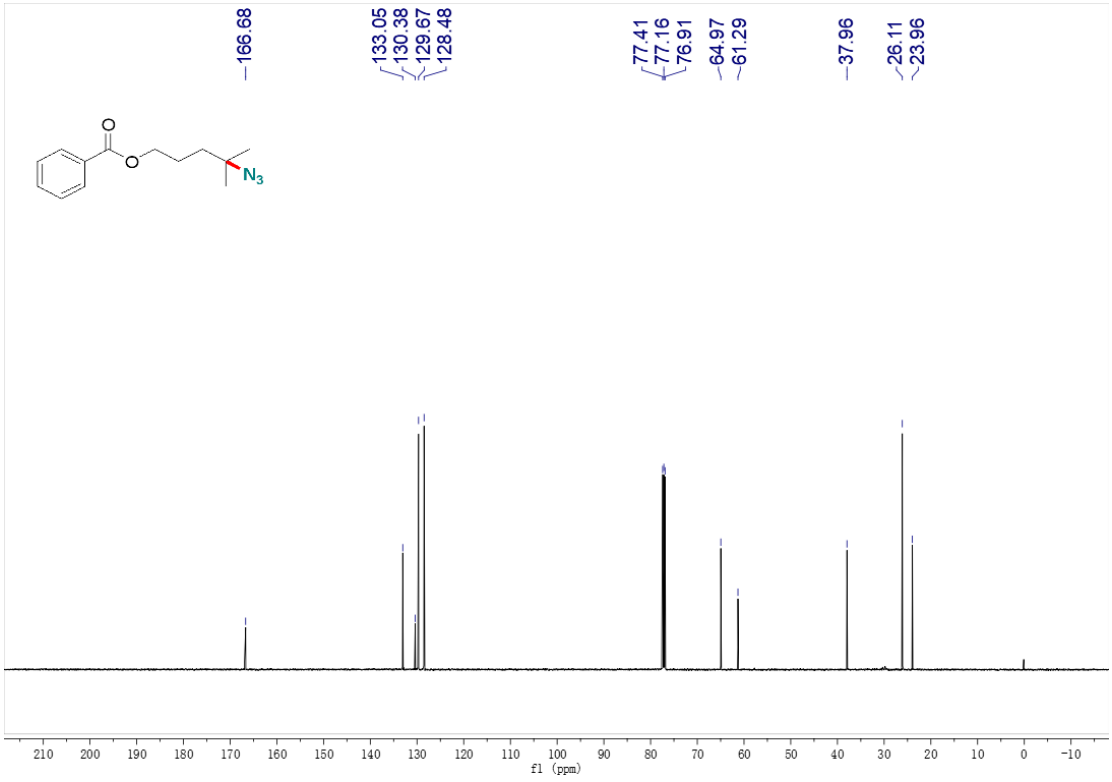
^{1}H NMR of compound **2b** (500 MHz, $CDCl_3$)



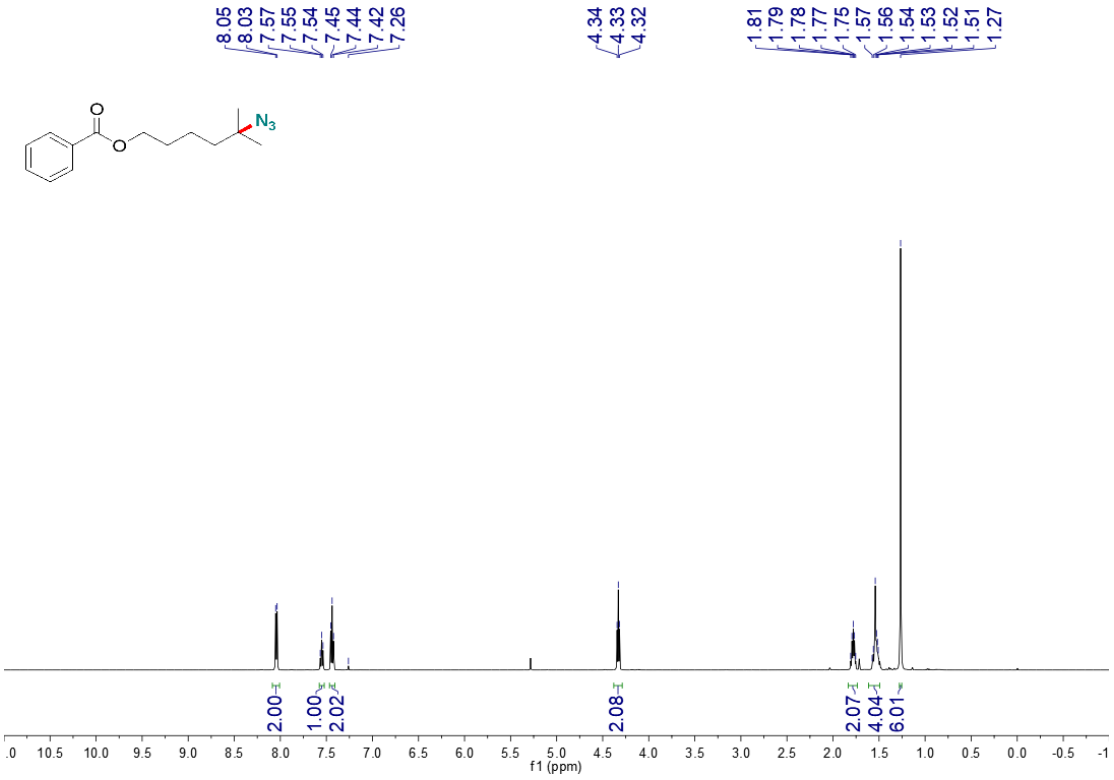
^{13}C NMR of compound **2b** (126 MHz, $CDCl_3$)



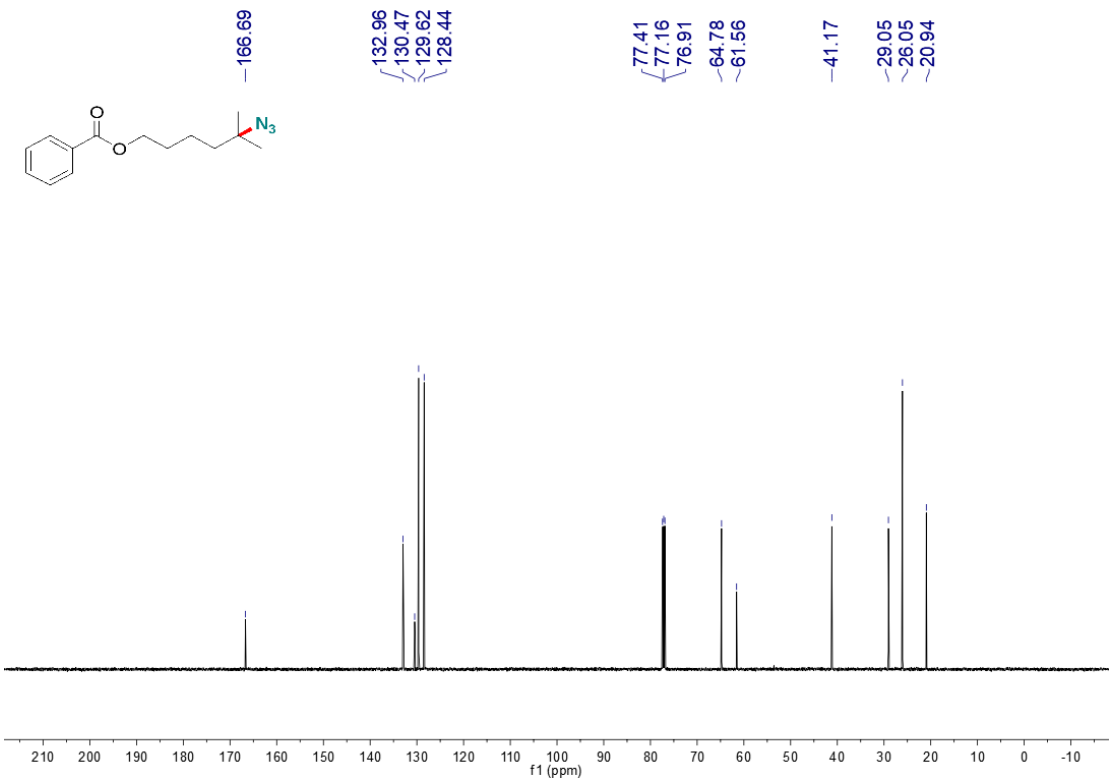
^{1}H NMR of compound **3b** (500 MHz, $CDCl_3$)



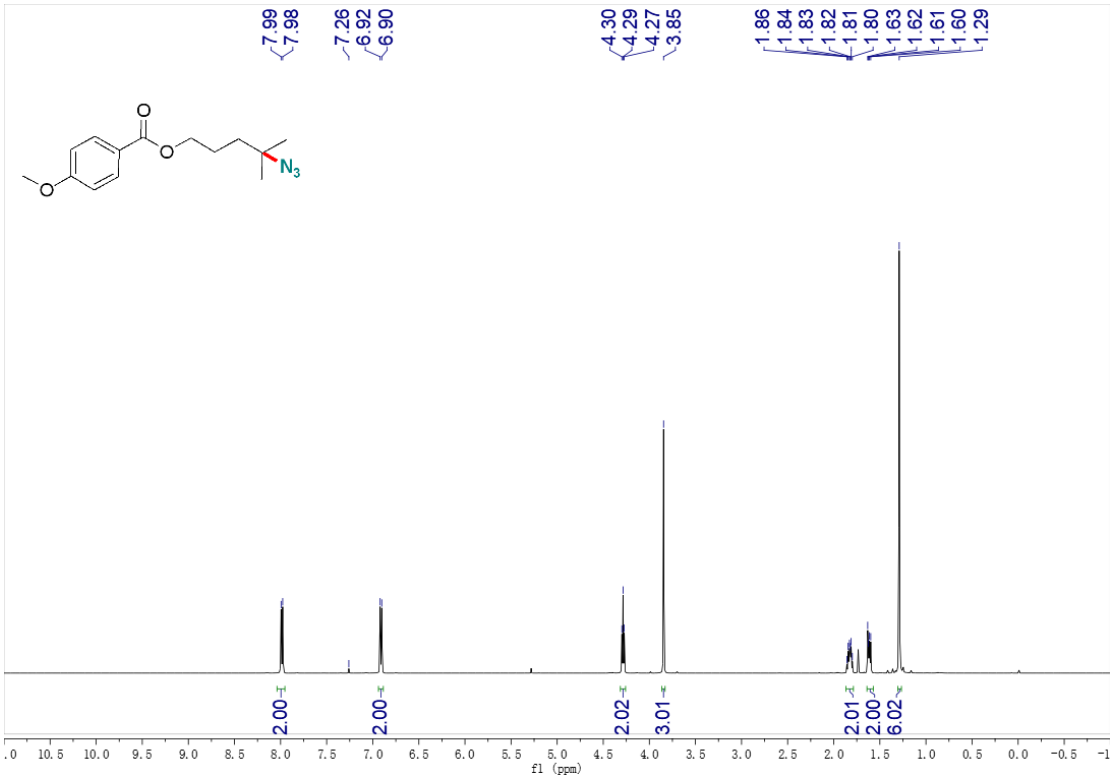
^{13}C NMR of compound **3b** (126 MHz, $CDCl_3$)



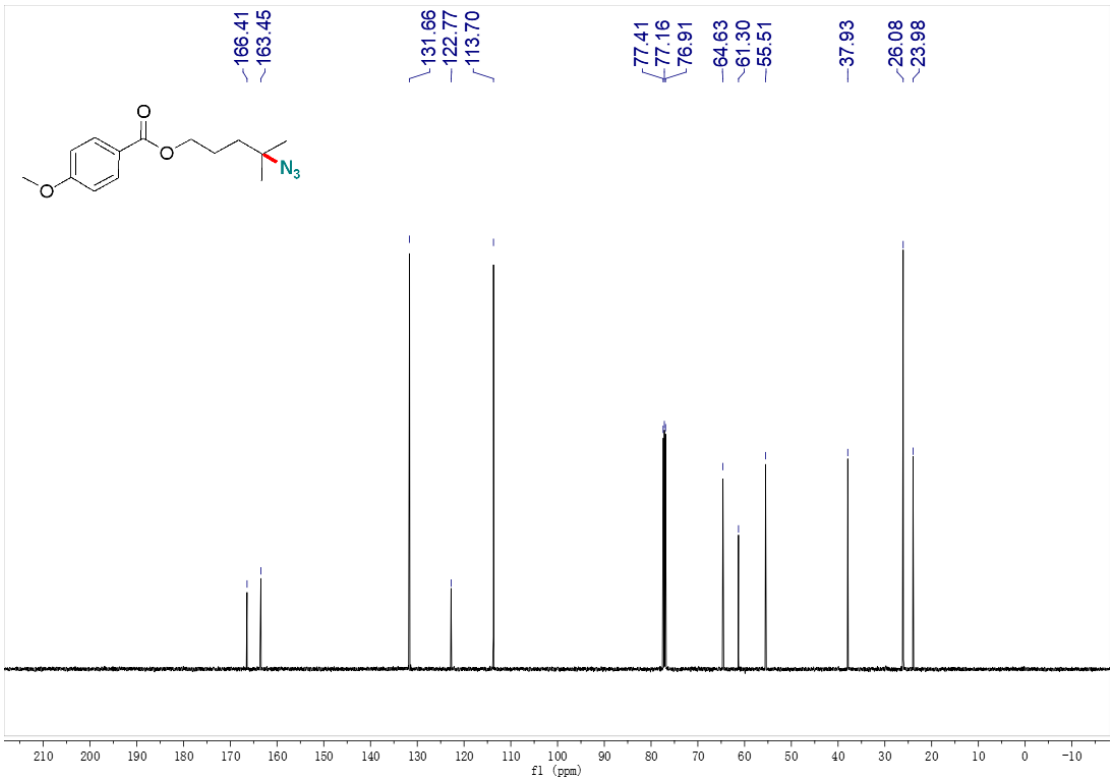
^{1}H NMR of compound **4b** (500 MHz, $CDCl_3$)



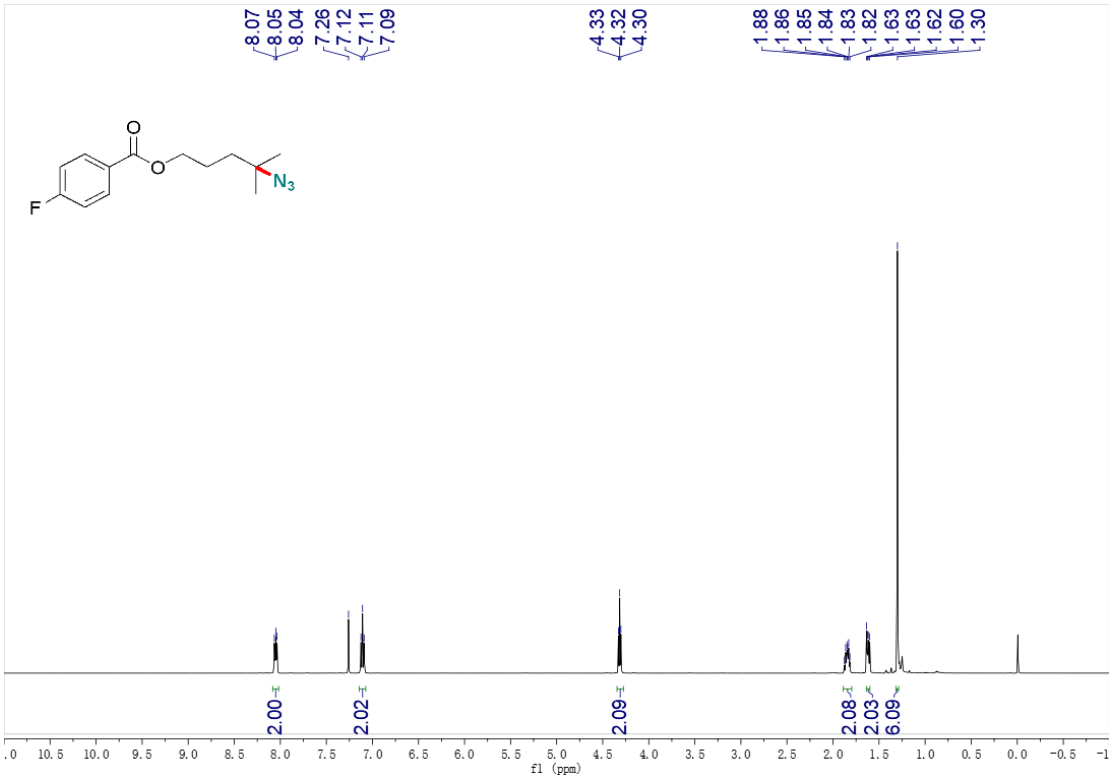
^{13}C NMR of compound **4b** (126 MHz, $CDCl_3$)



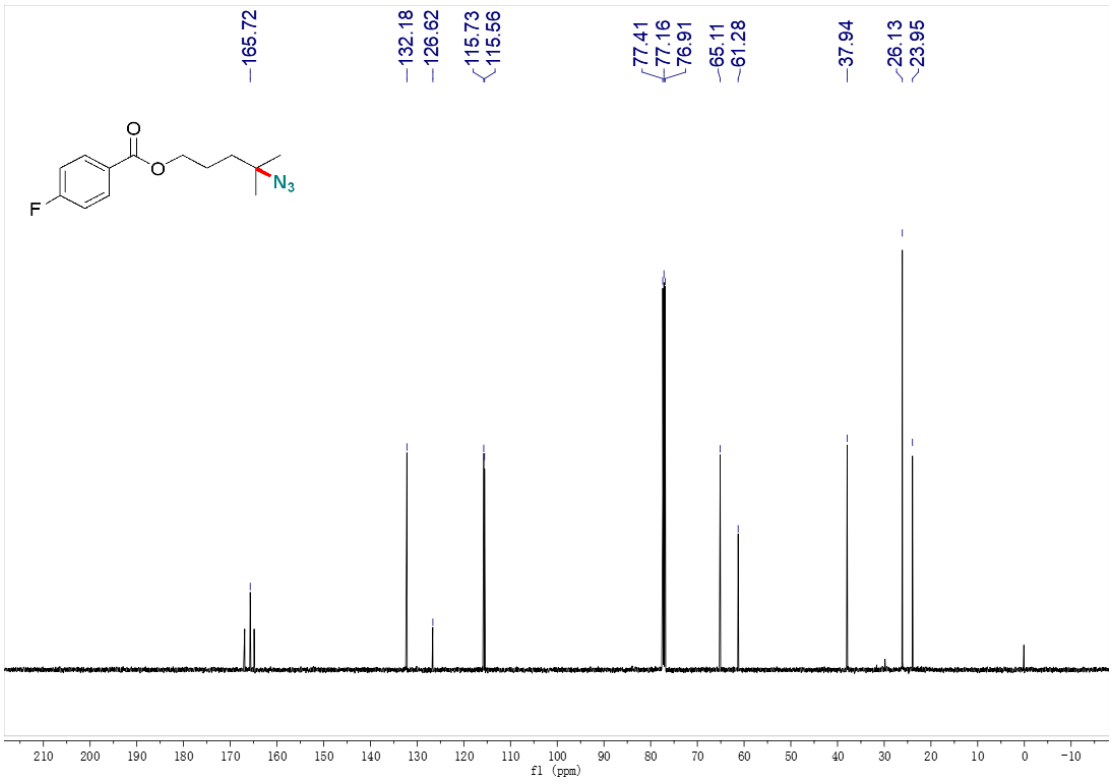
^{1}H NMR of compound **5b** (500 MHz, $CDCl_3$)



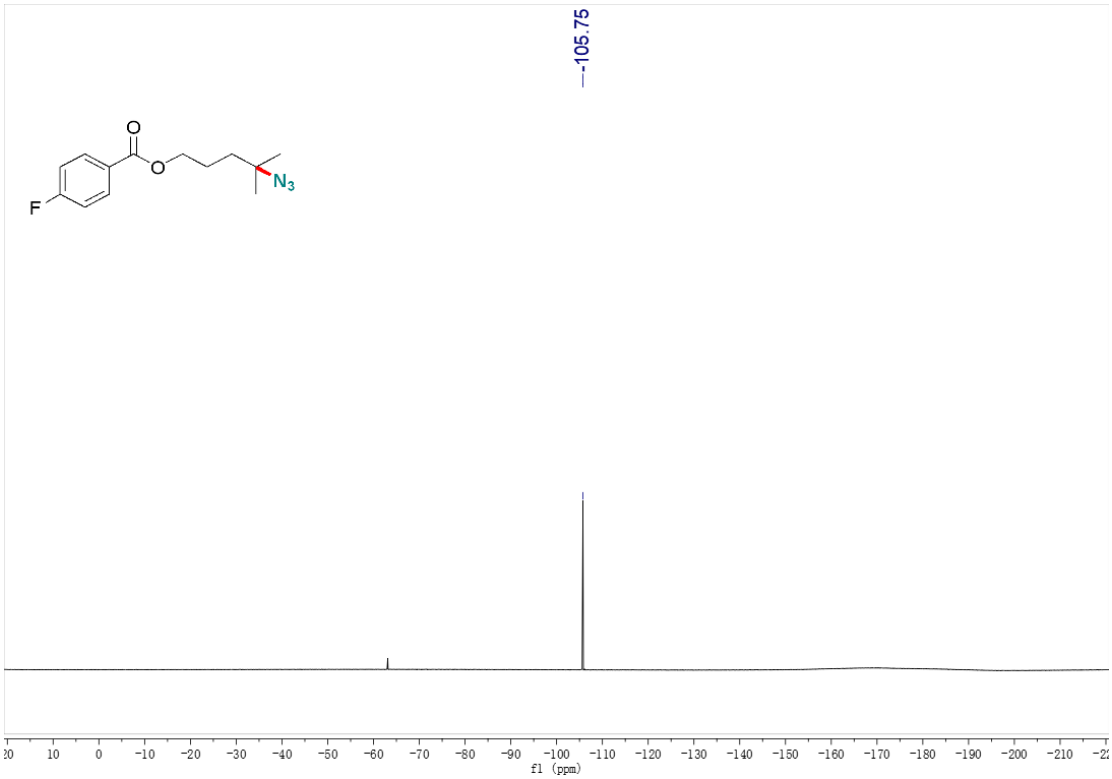
^{13}C NMR of compound **5b** (126 MHz, $CDCl_3$)



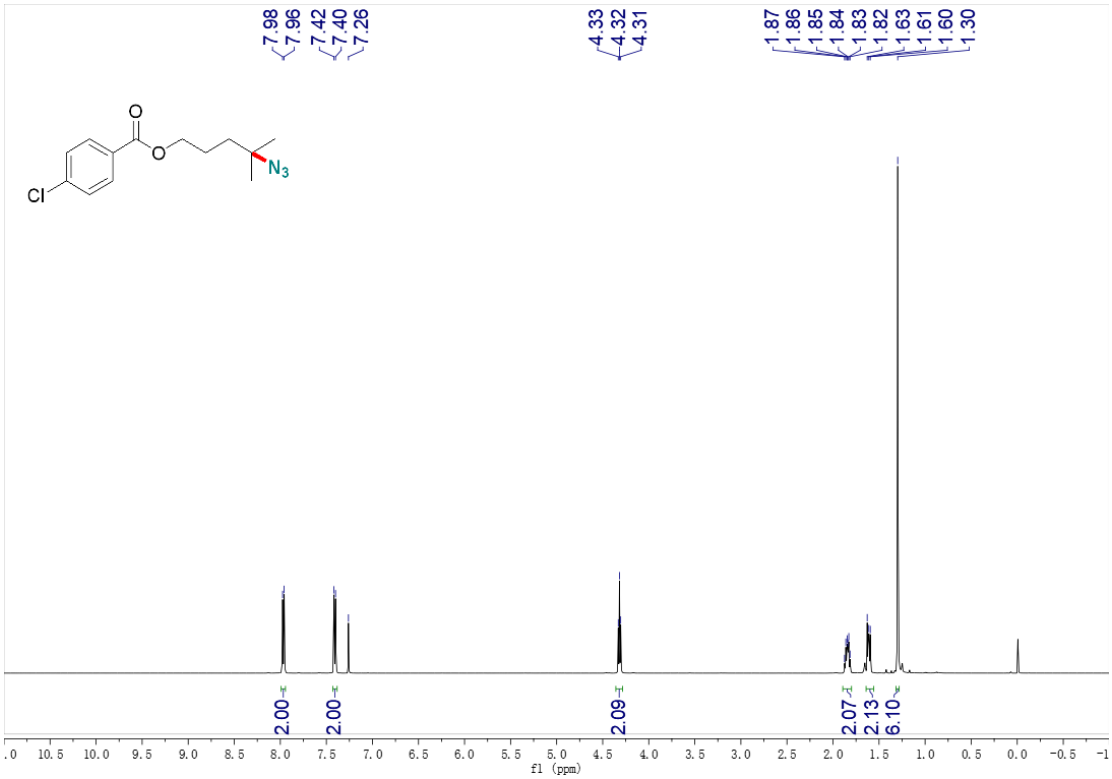
^{1}H NMR of compound **6b** (500 MHz, $CDCl_3$)



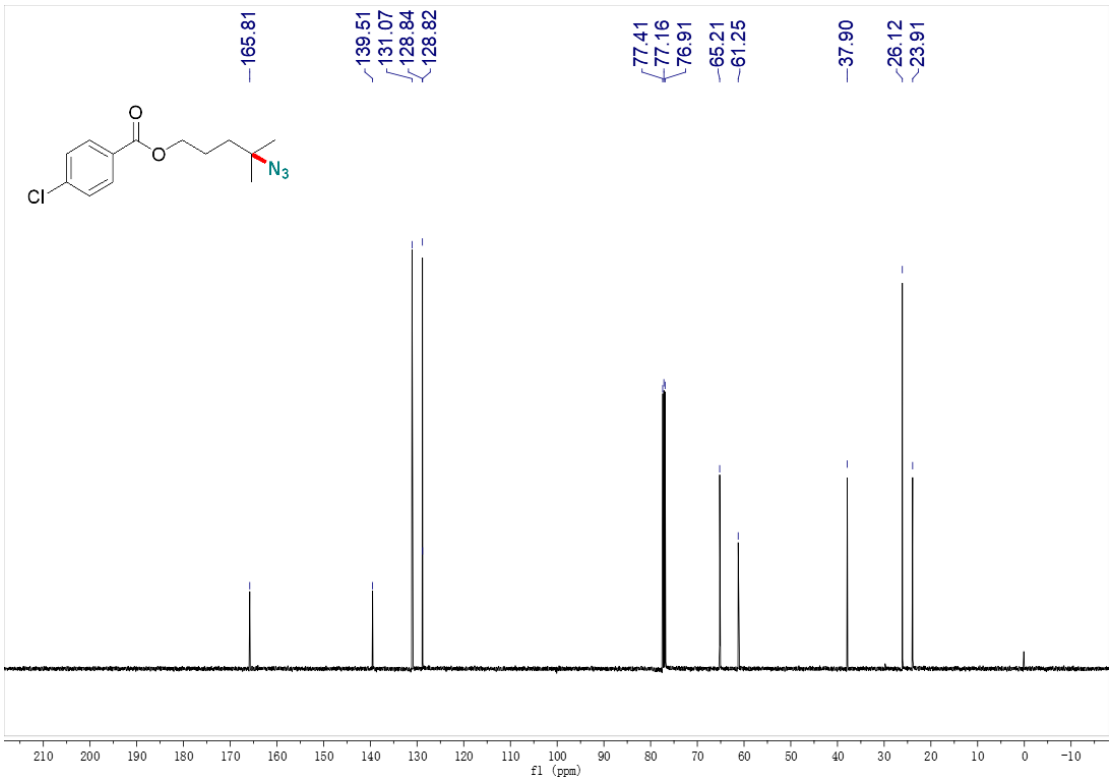
^{13}C NMR of compound **6b** (126 MHz, $CDCl_3$)



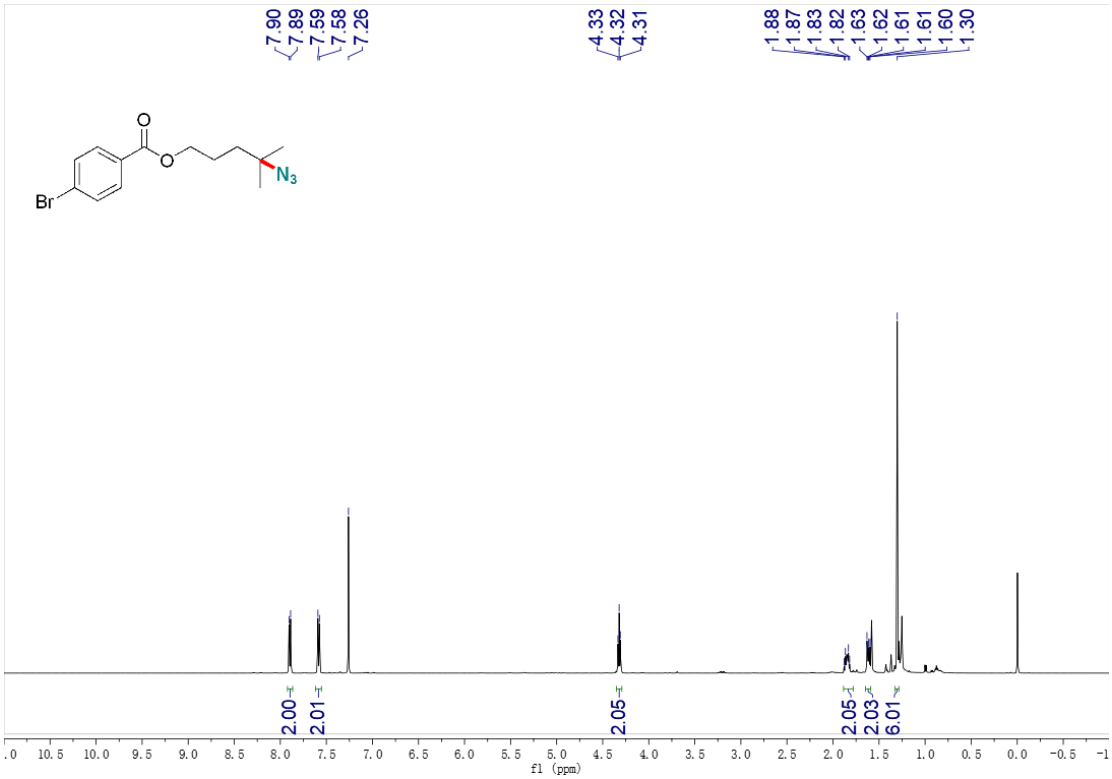
^{19}F NMR of compound **6b** (471 MHz, $CDCl_3$)



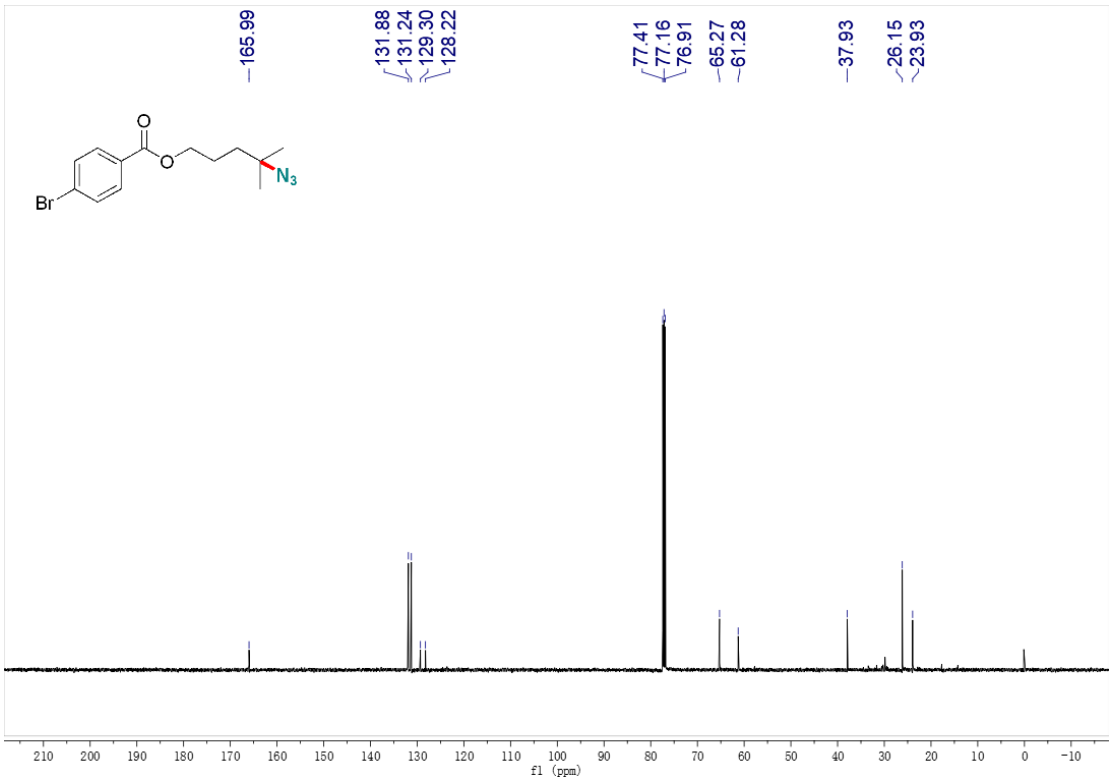
^{1}H NMR of compound **7b** (500 MHz, $CDCl_3$)



^{13}C NMR of compound **7b** (126 MHz, $CDCl_3$)



^{1}H NMR of compound **8b** (500 MHz, $CDCl_3$)



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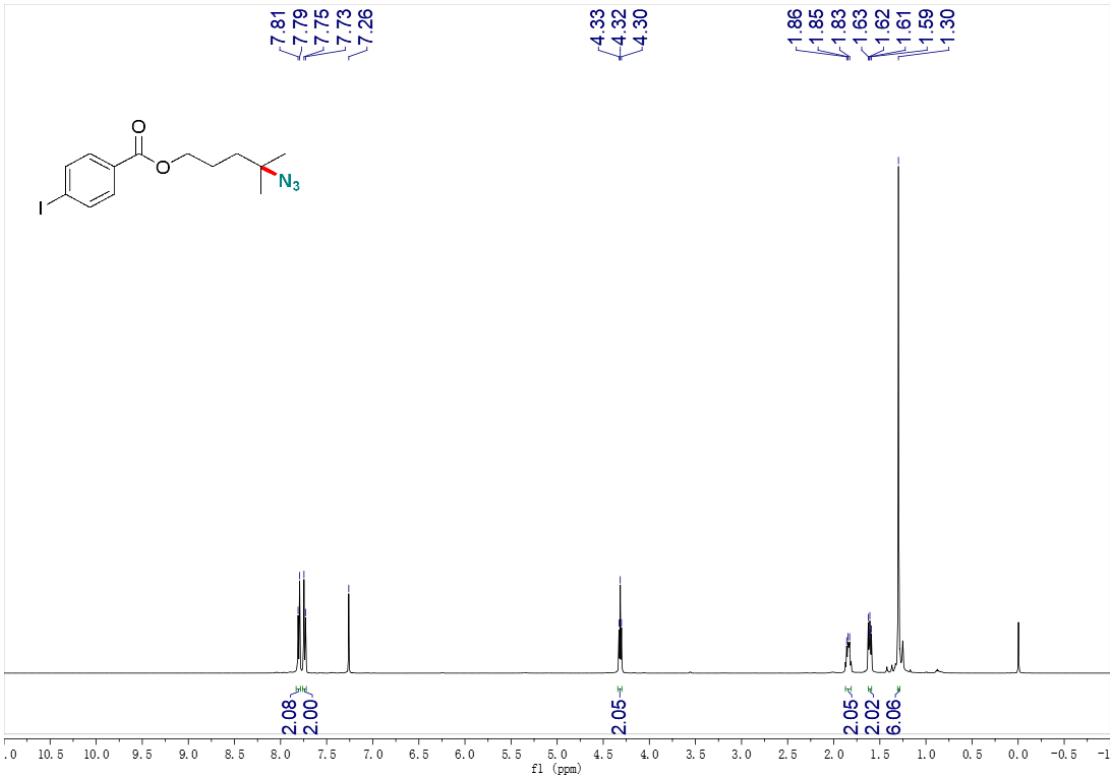
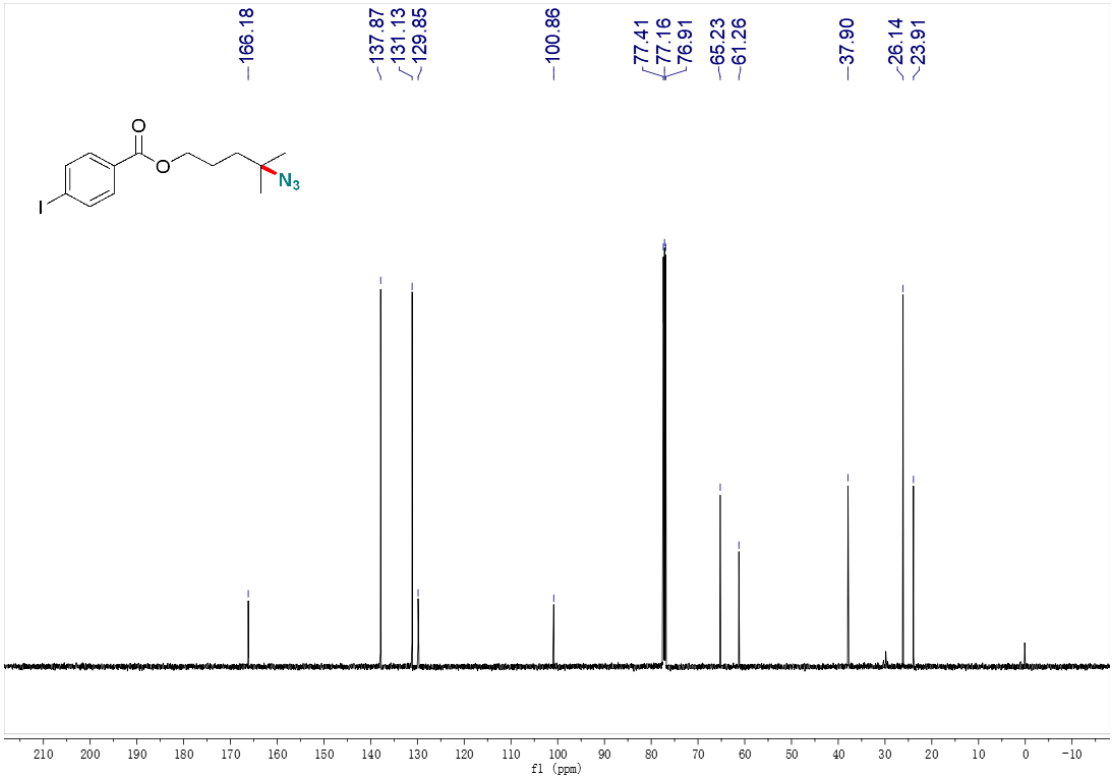
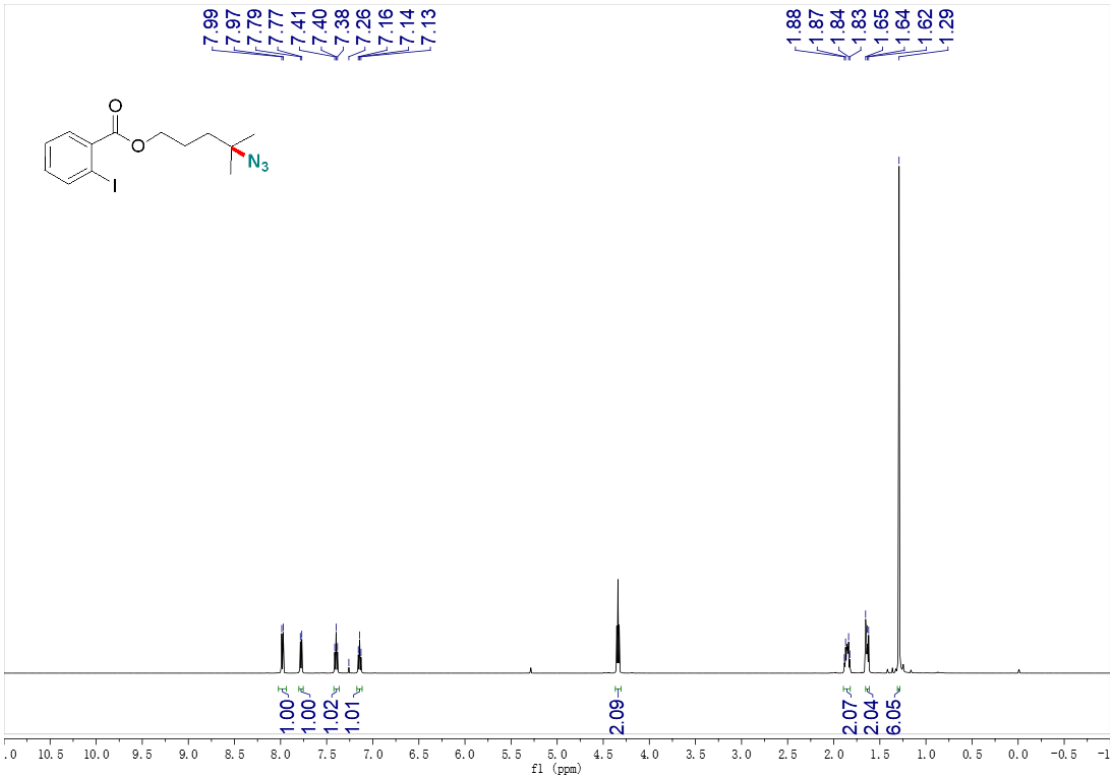


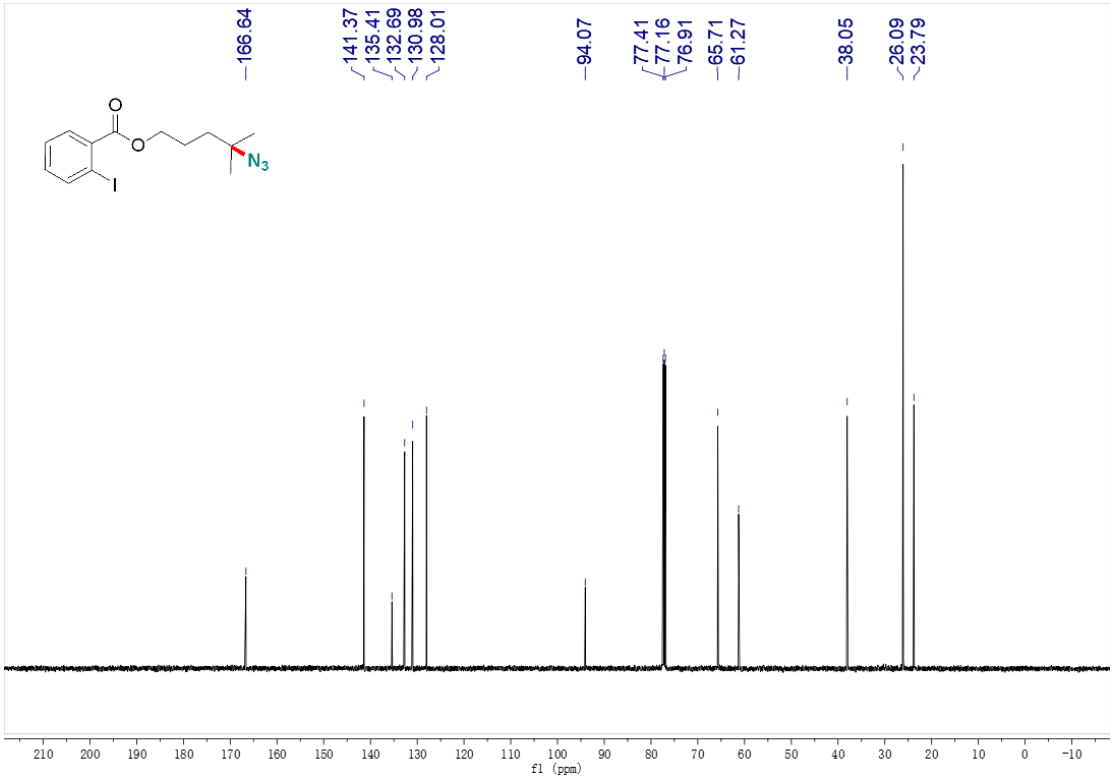
^{1}H NMR of compound **9b** (500 MHz, $CDCl_3$)



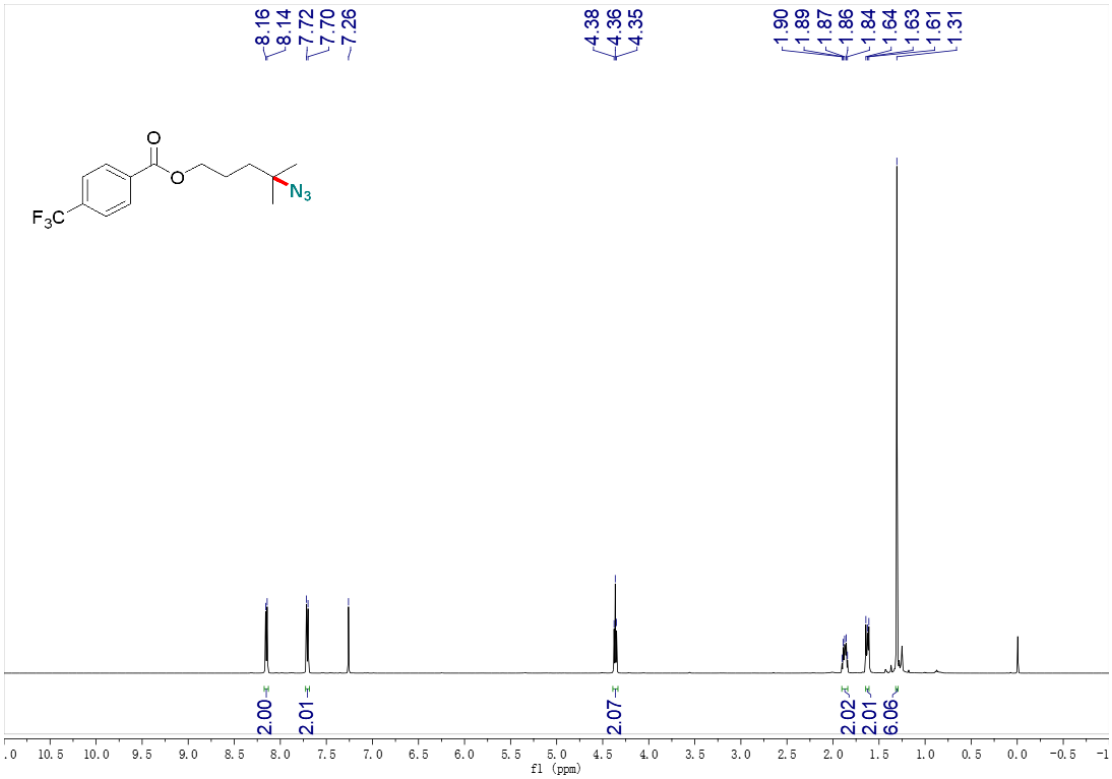
^{13}C NMR of compound **9b** (126 MHz, $CDCl_3$)



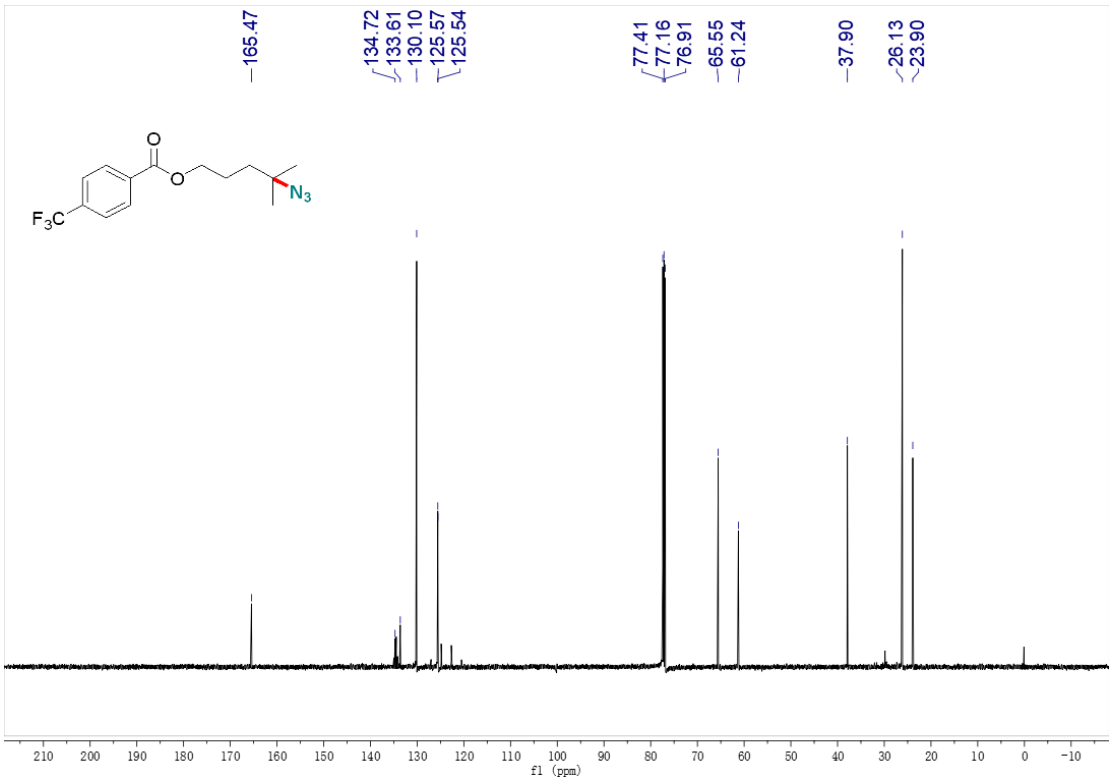
^{1}H NMR of compound **10b** (500 MHz, $CDCl_3$)



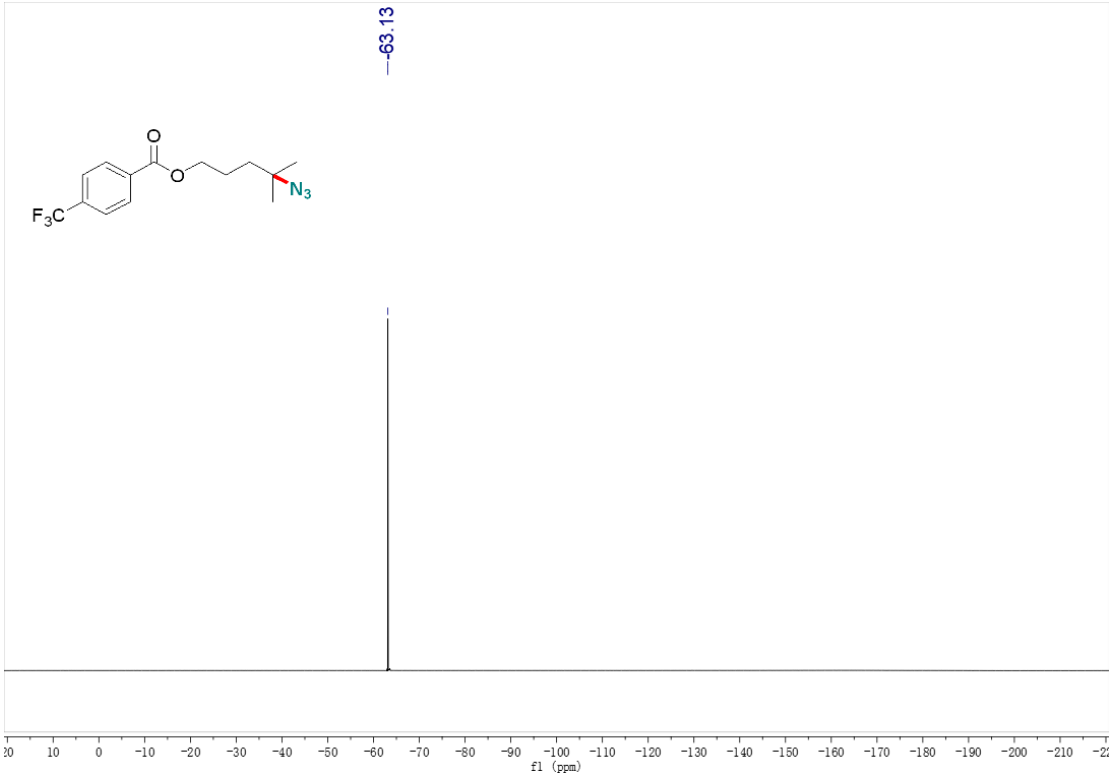
^{13}C NMR of compound **10b** (126 MHz, $CDCl_3$)



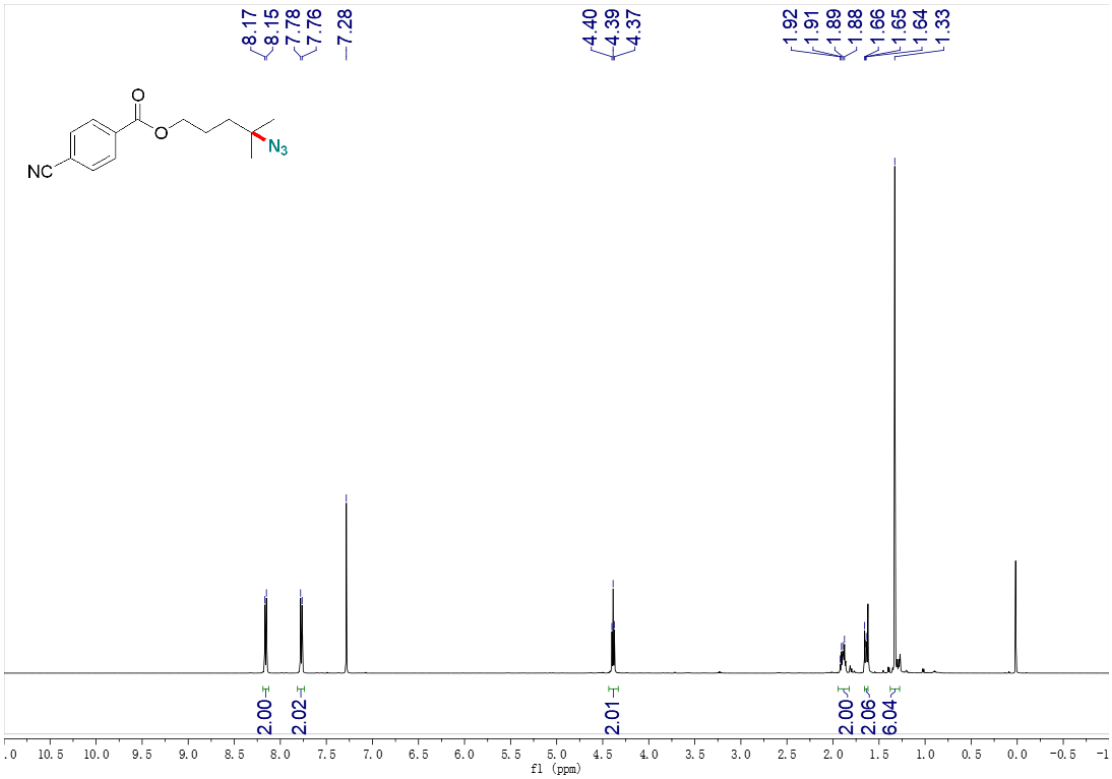
^{1}H NMR of compound **11b** (500 MHz, $CDCl_3$)



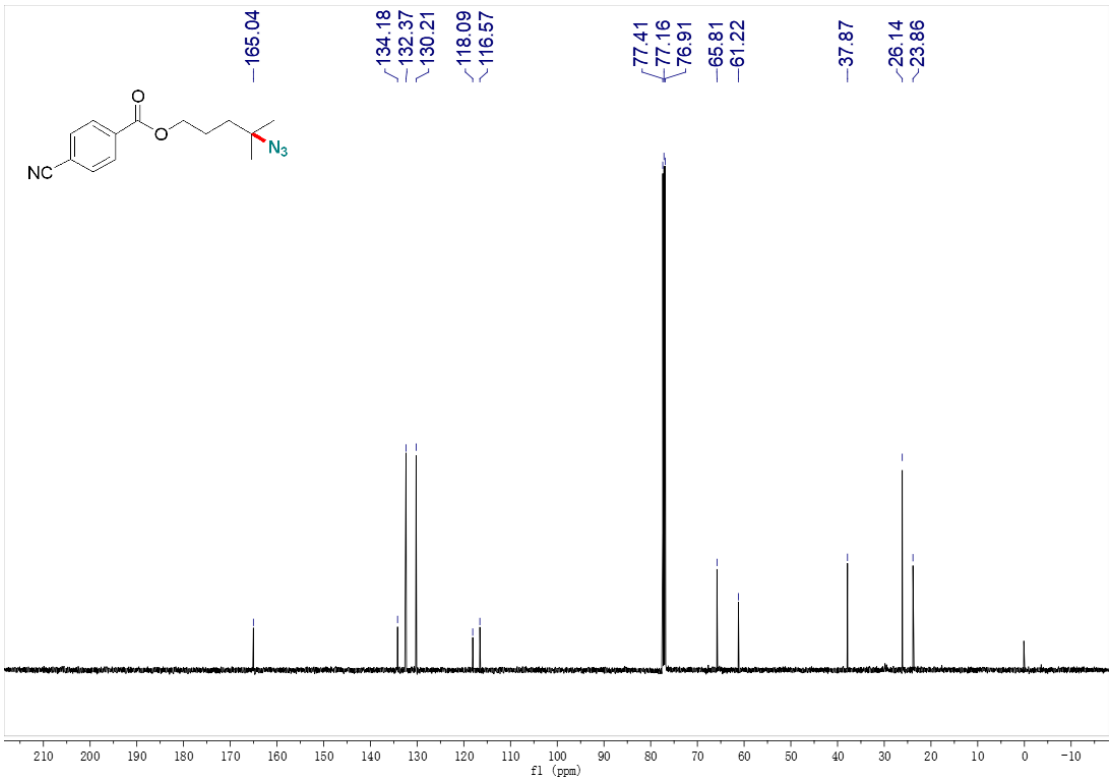
^{13}C NMR of compound **11b** (126 MHz, $CDCl_3$)



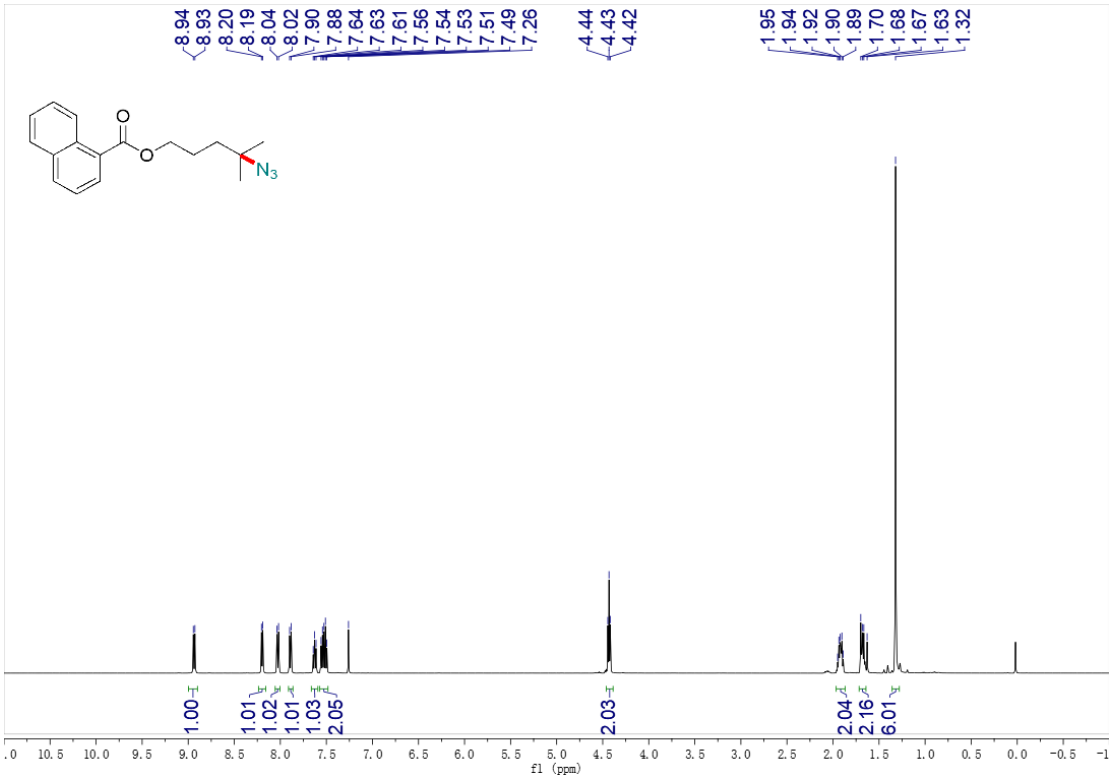
^{19}F NMR of compound **11b** (471 MHz, $CDCl_3$)



^{1}H NMR of compound **12b** (500 MHz, $CDCl_3$)



^{13}C NMR of compound **12b** (126 MHz, $CDCl_3$)



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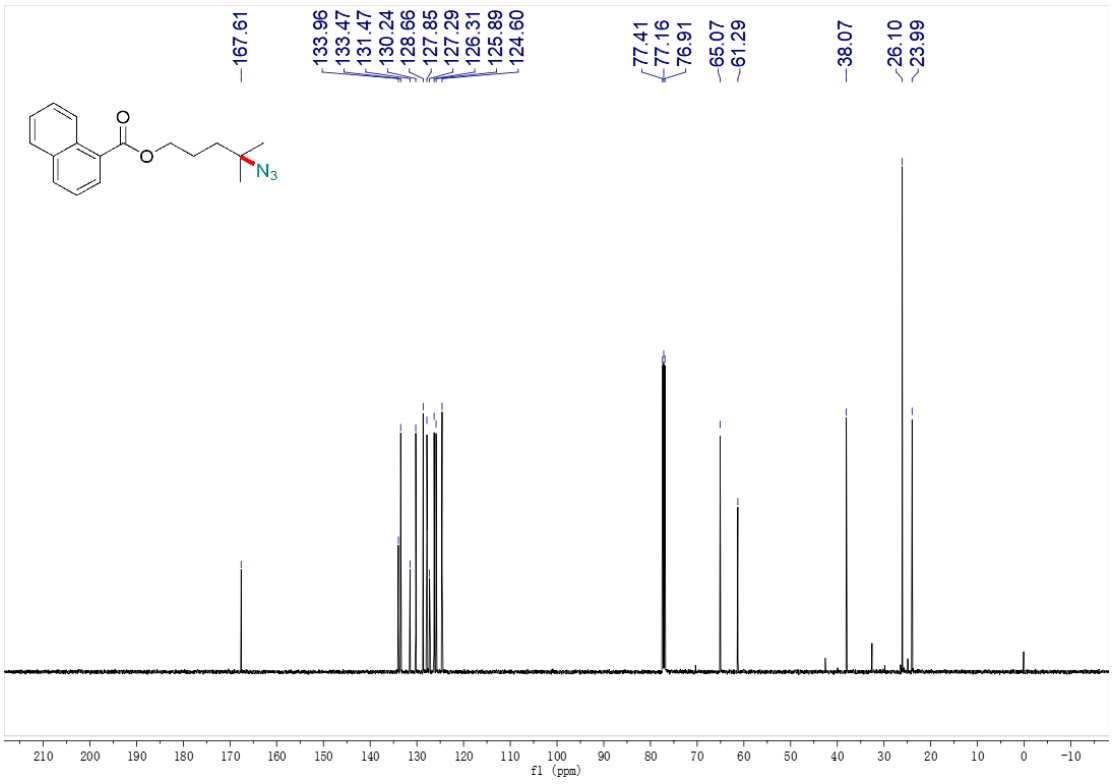
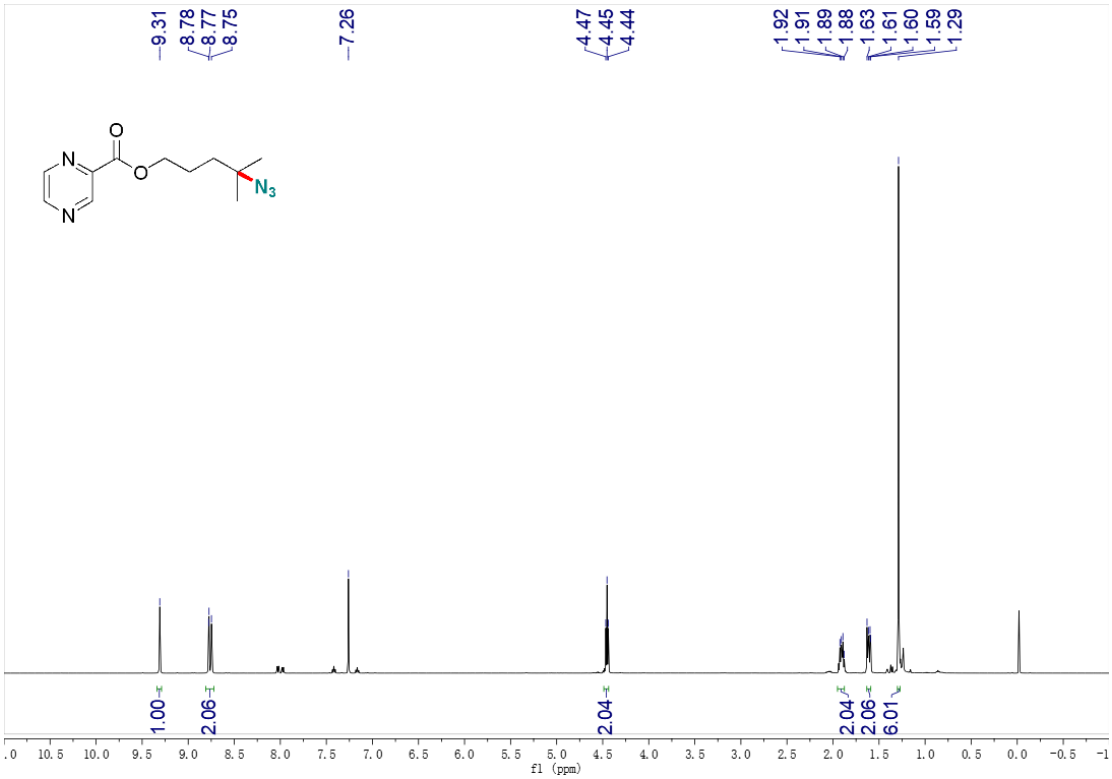
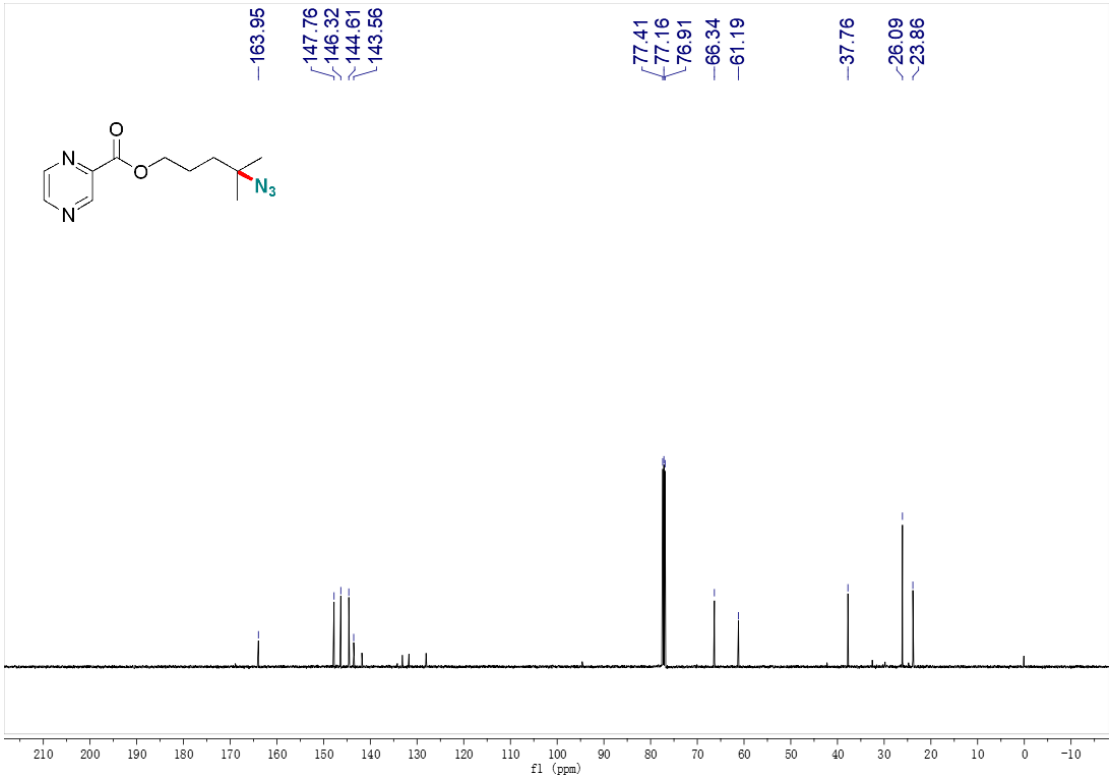


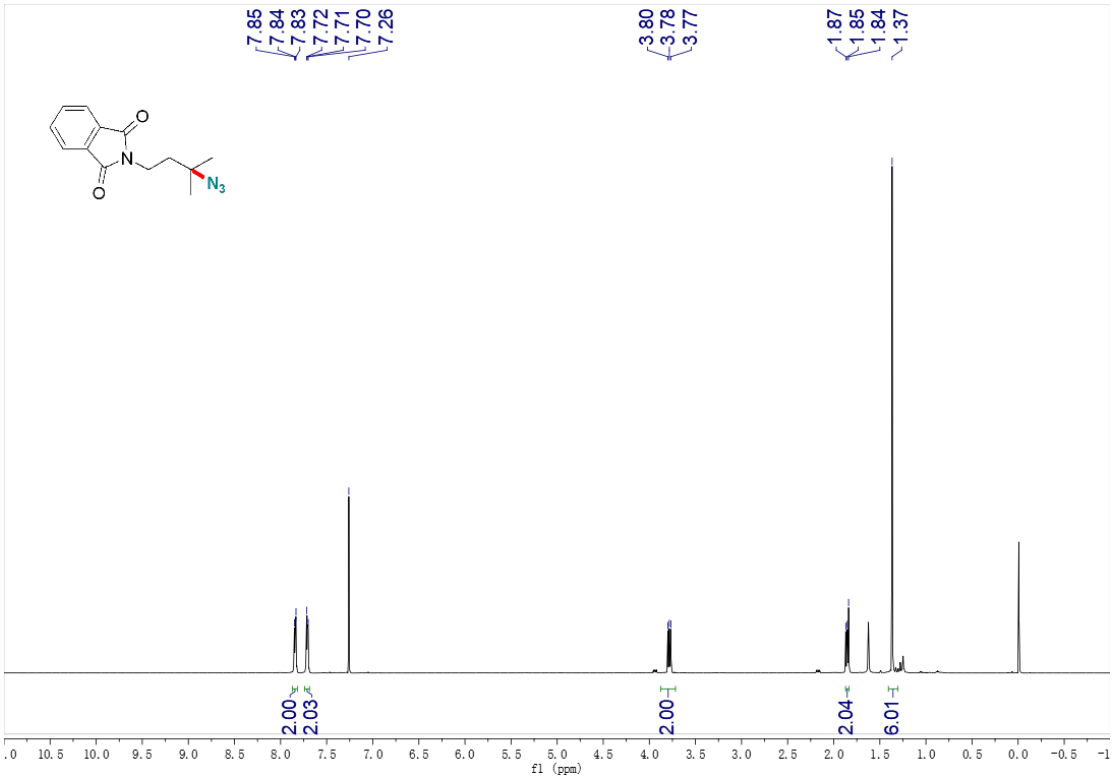
^{13}C NMR of compound **13b** (126 MHz, $CDCl_3$)



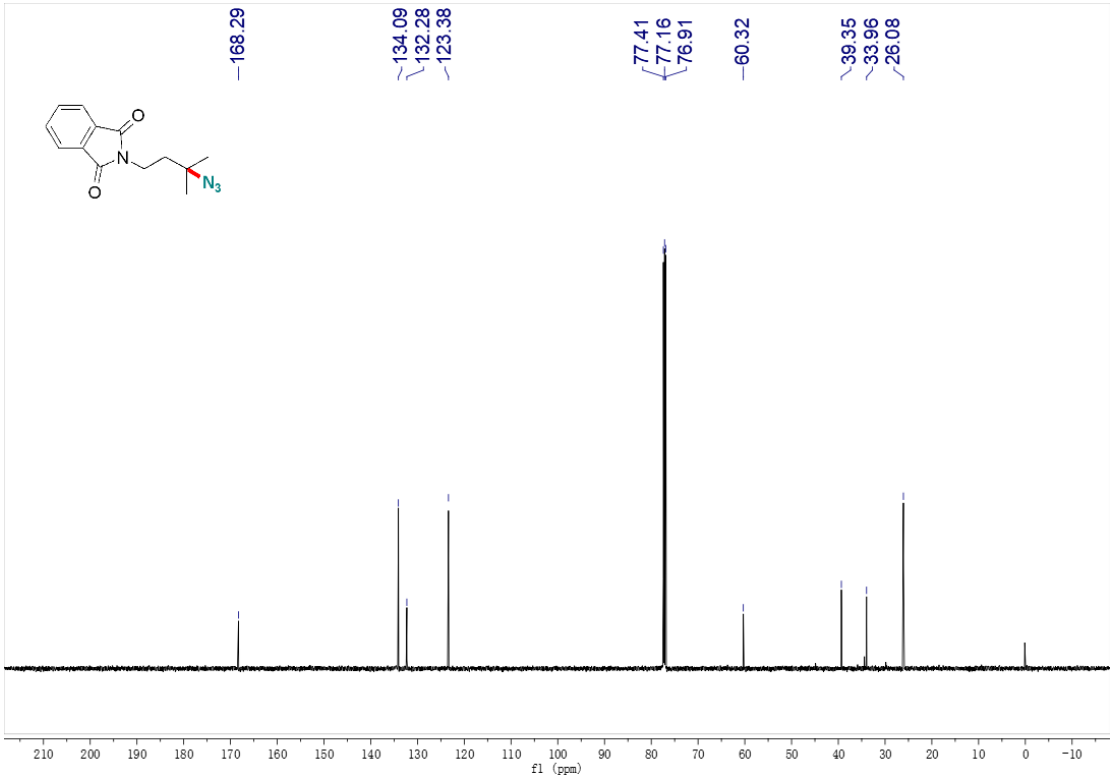
^{1}H NMR of compound **14b** (500 MHz, $CDCl_3$)



^{13}C NMR of compound **14b** (126 MHz, $CDCl_3$)



^{1}H NMR of compound **15b** (500 MHz, $CDCl_3$)



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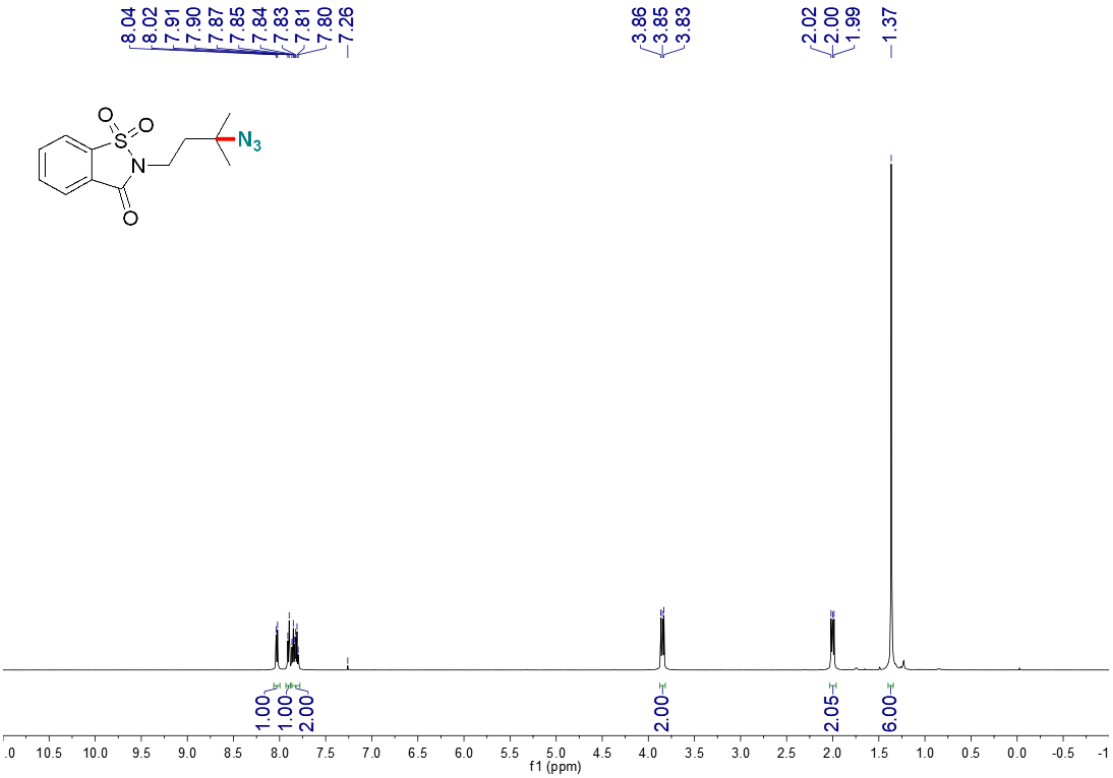

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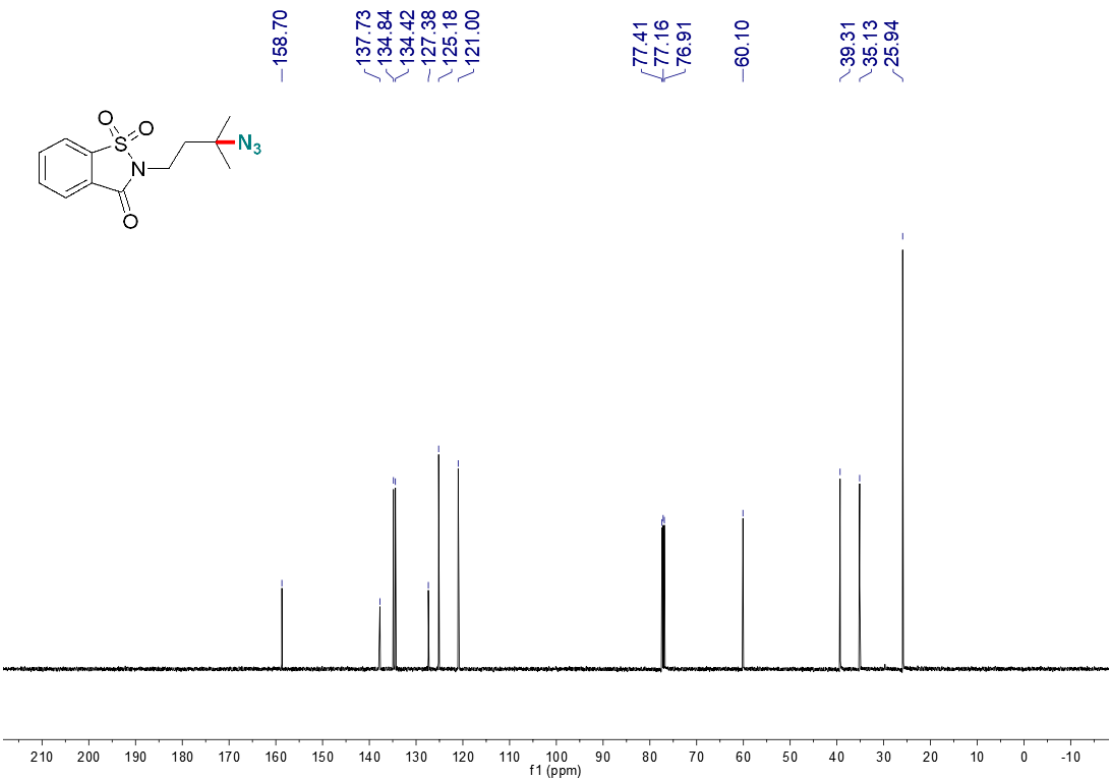
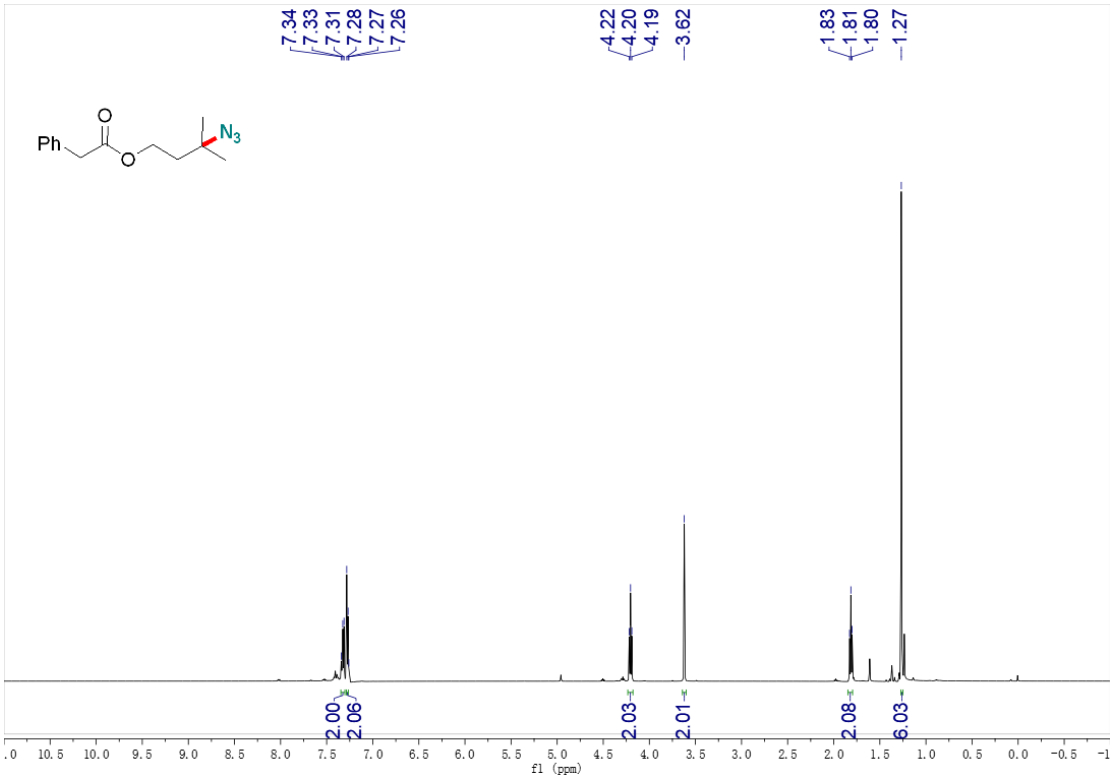
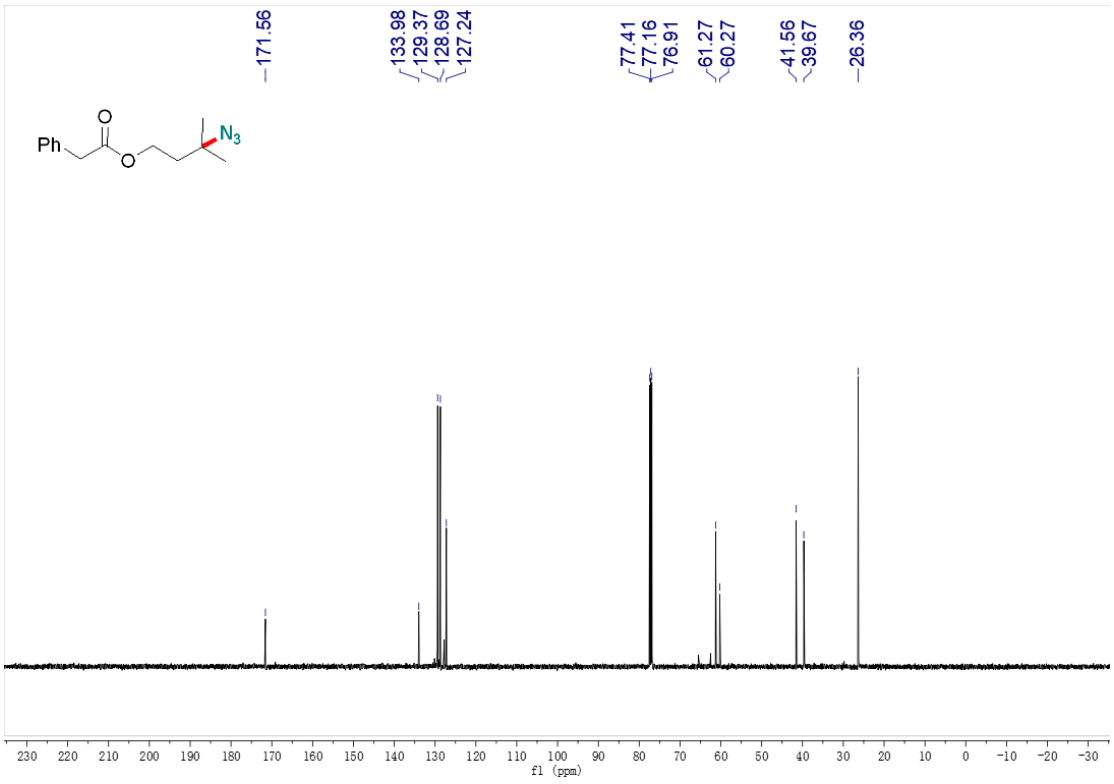


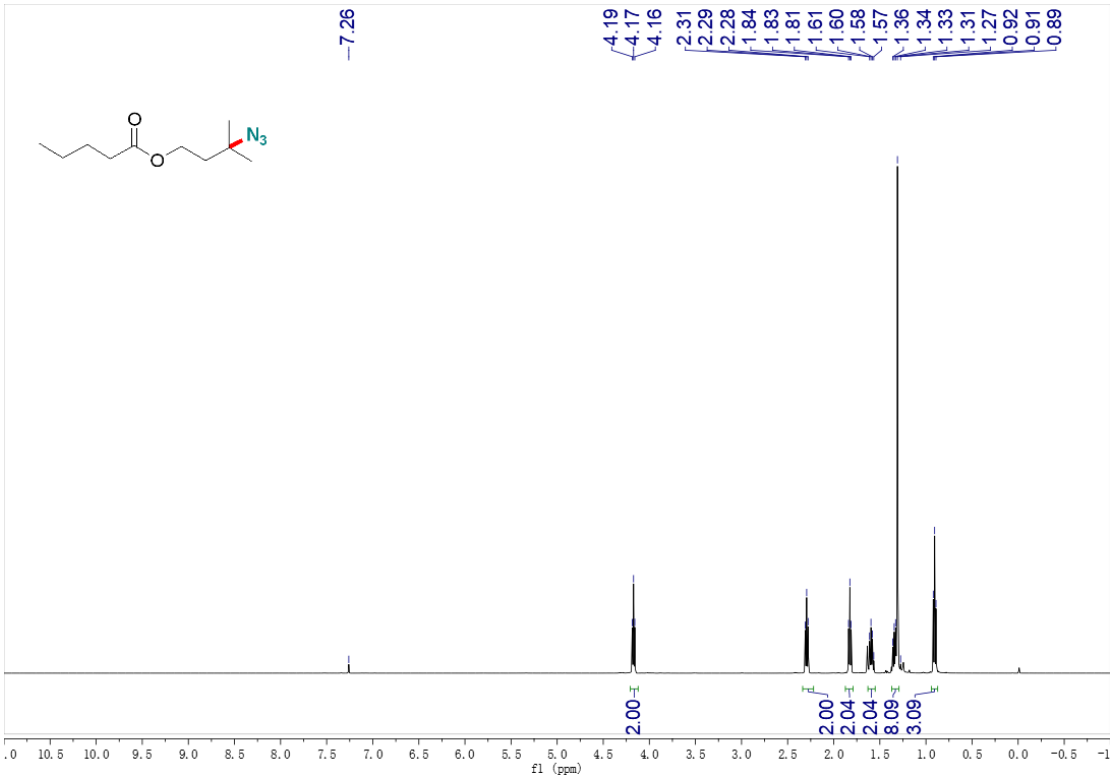
^{13}C NMR of compound **16b** (126 MHz, $CDCl_3$)



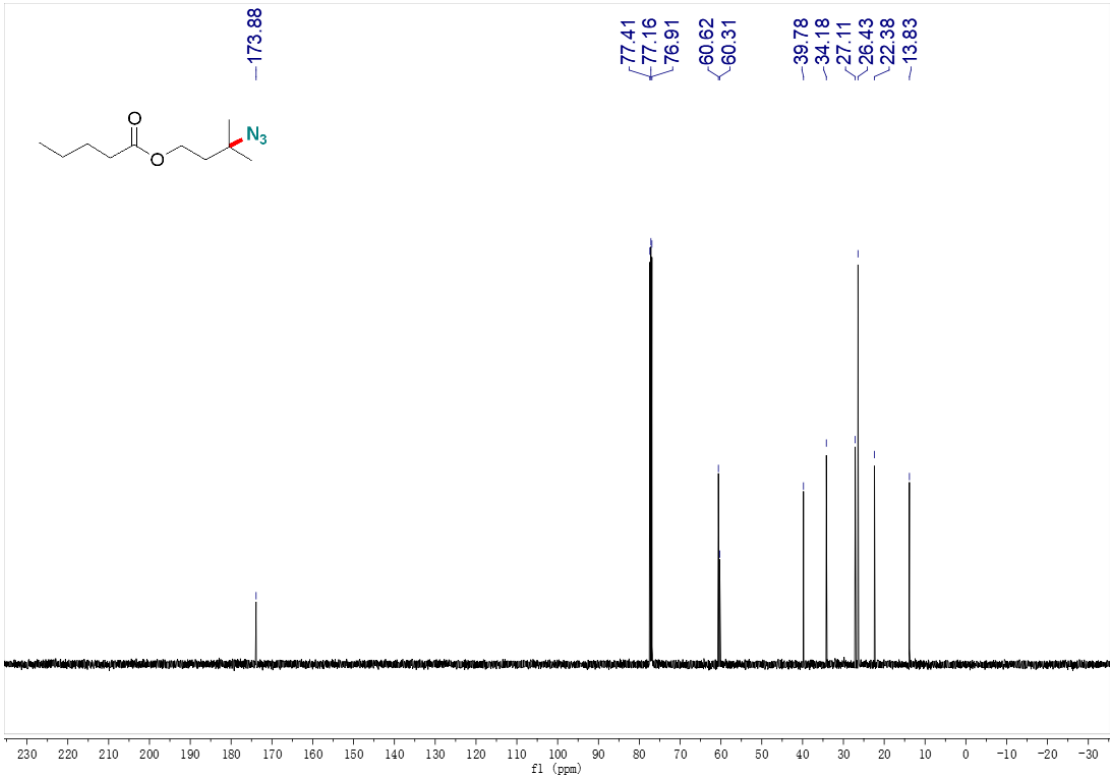
^{1}H NMR of compound **17b** (500 MHz, $CDCl_3$)



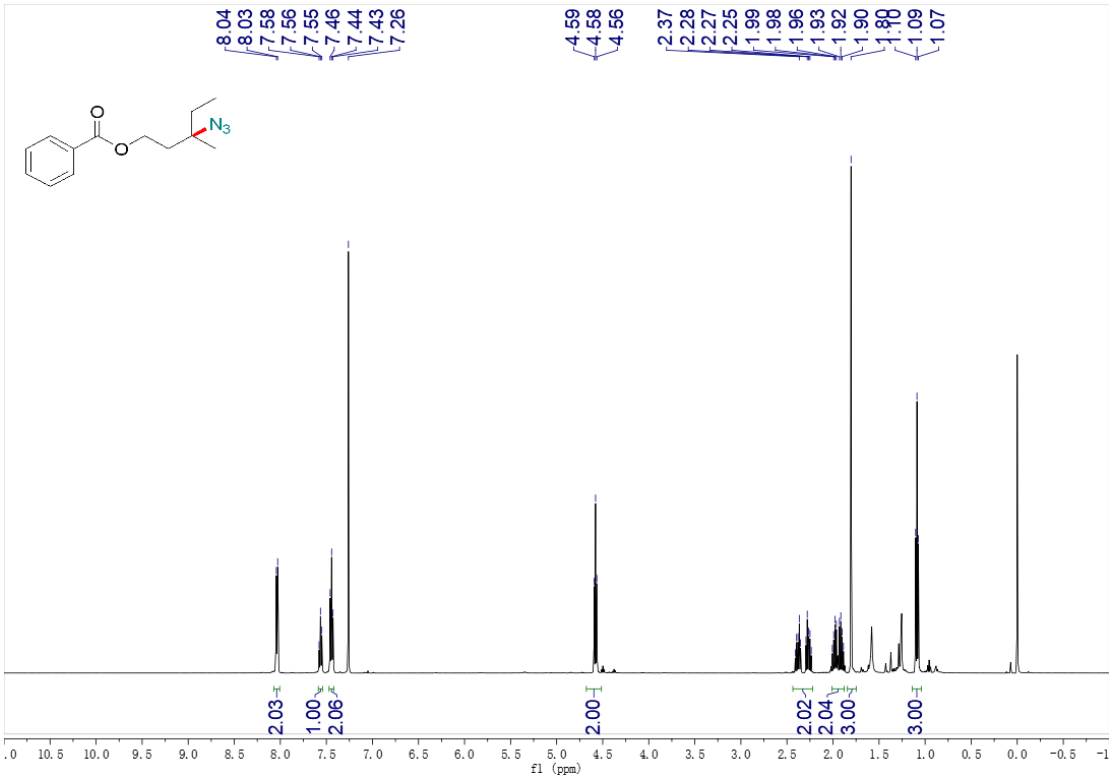
^{13}C NMR of compound **17b** (126 MHz, $CDCl_3$)



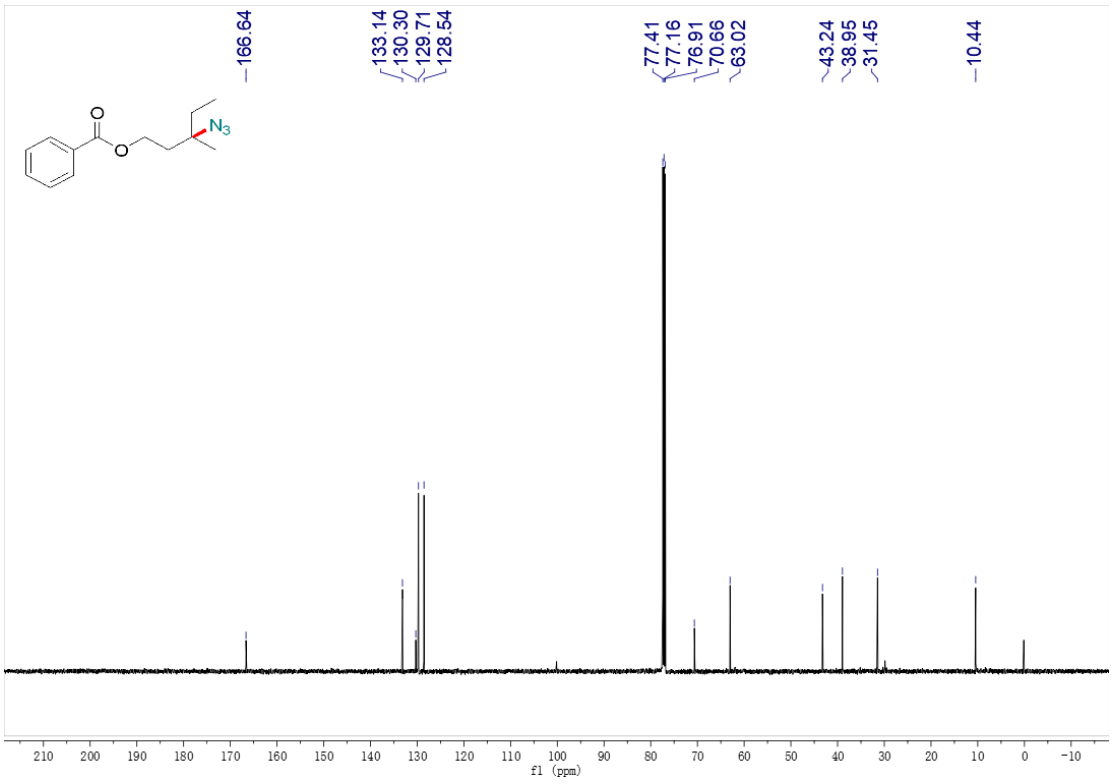
^{1}H NMR of compound **18b** (500 MHz, $CDCl_3$)



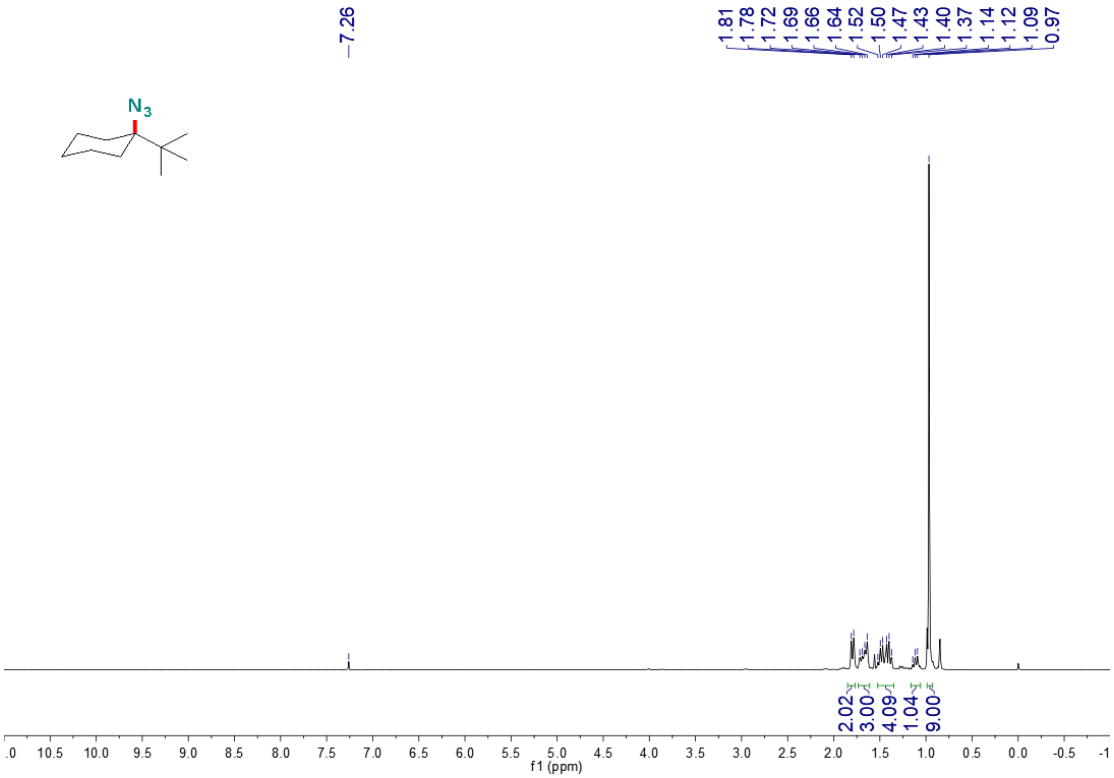
^{13}C NMR of compound **18b** (126 MHz, $CDCl_3$)



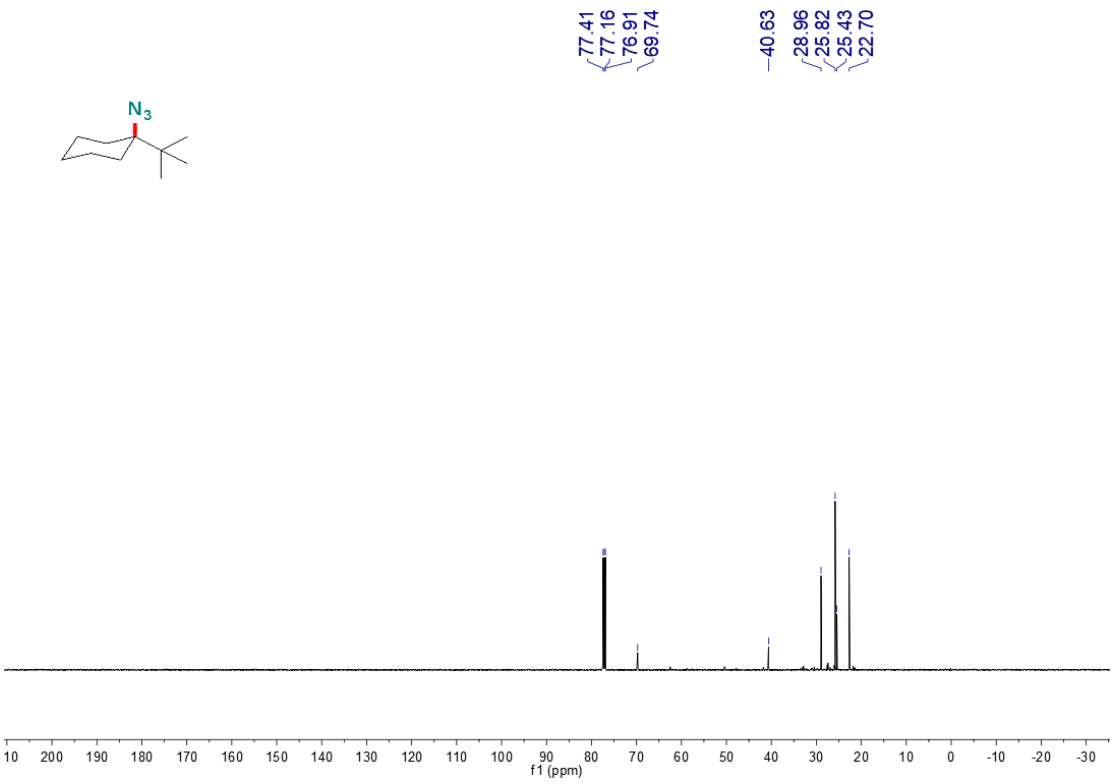
^{1}H NMR of compound **19b** (500 MHz, $CDCl_3$)



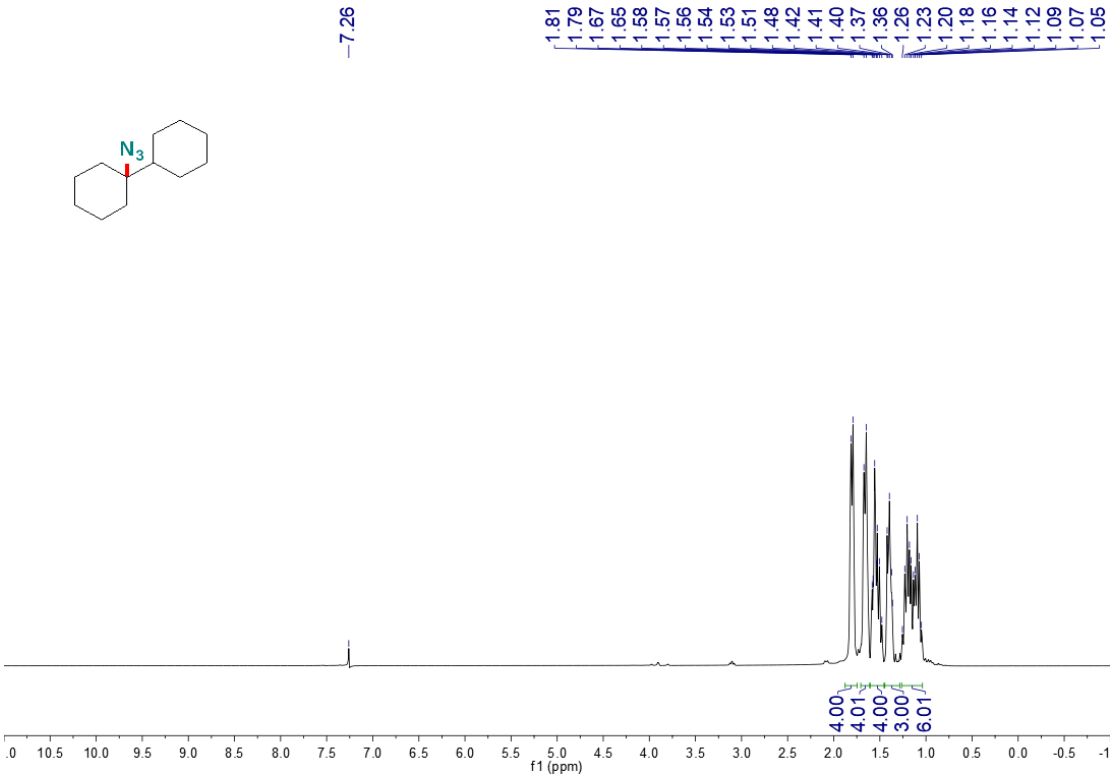
^{13}C NMR of compound **19b** (126 MHz, $CDCl_3$)



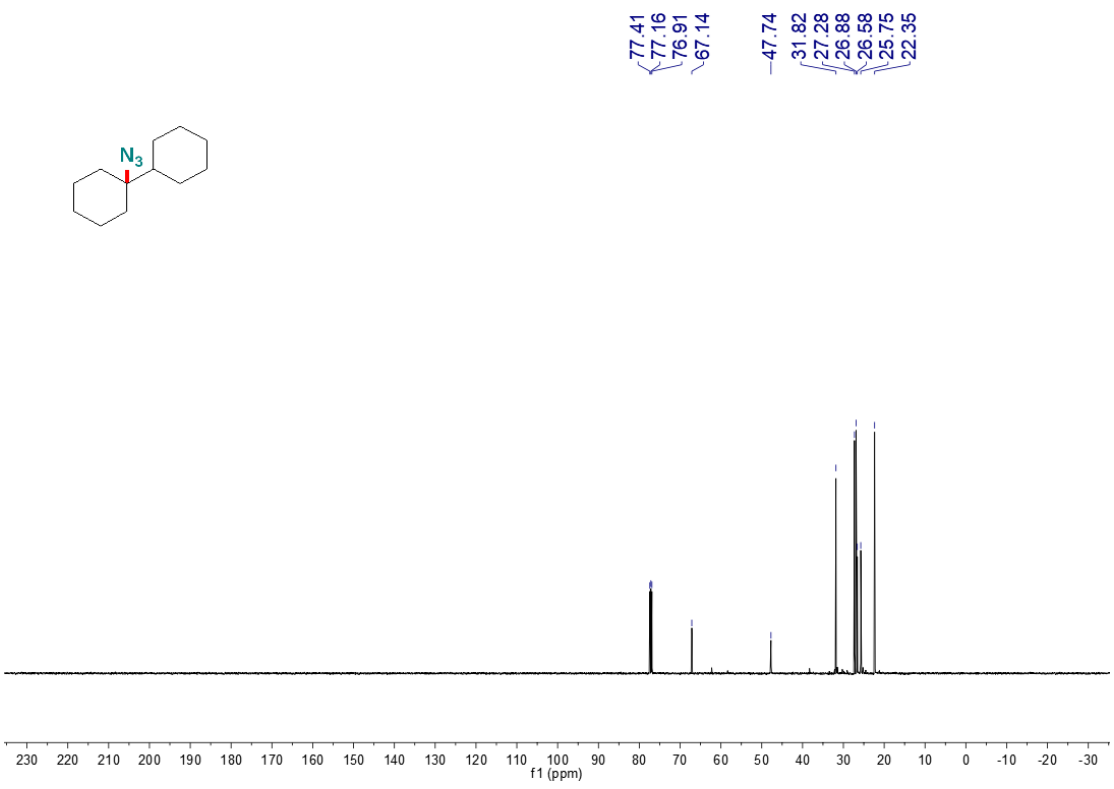
^{1}H NMR of compound **20b** (500 MHz, $CDCl_3$)



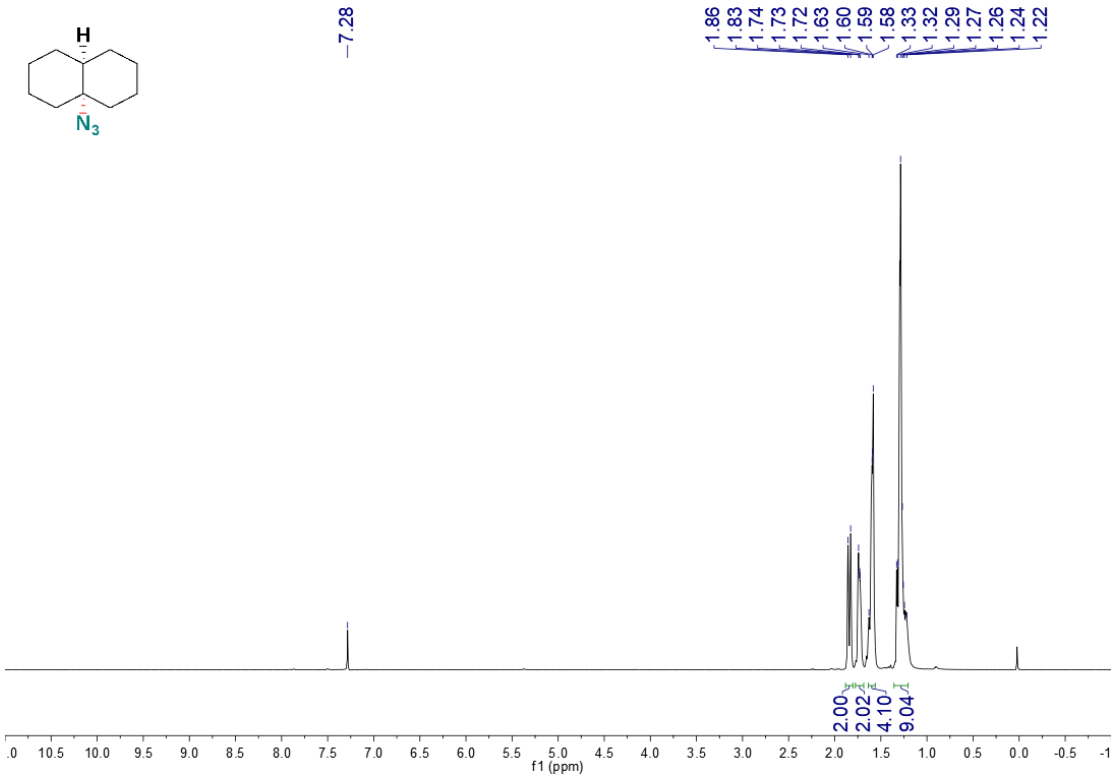
^{13}C NMR of compound **20b** (126 MHz, $CDCl_3$)



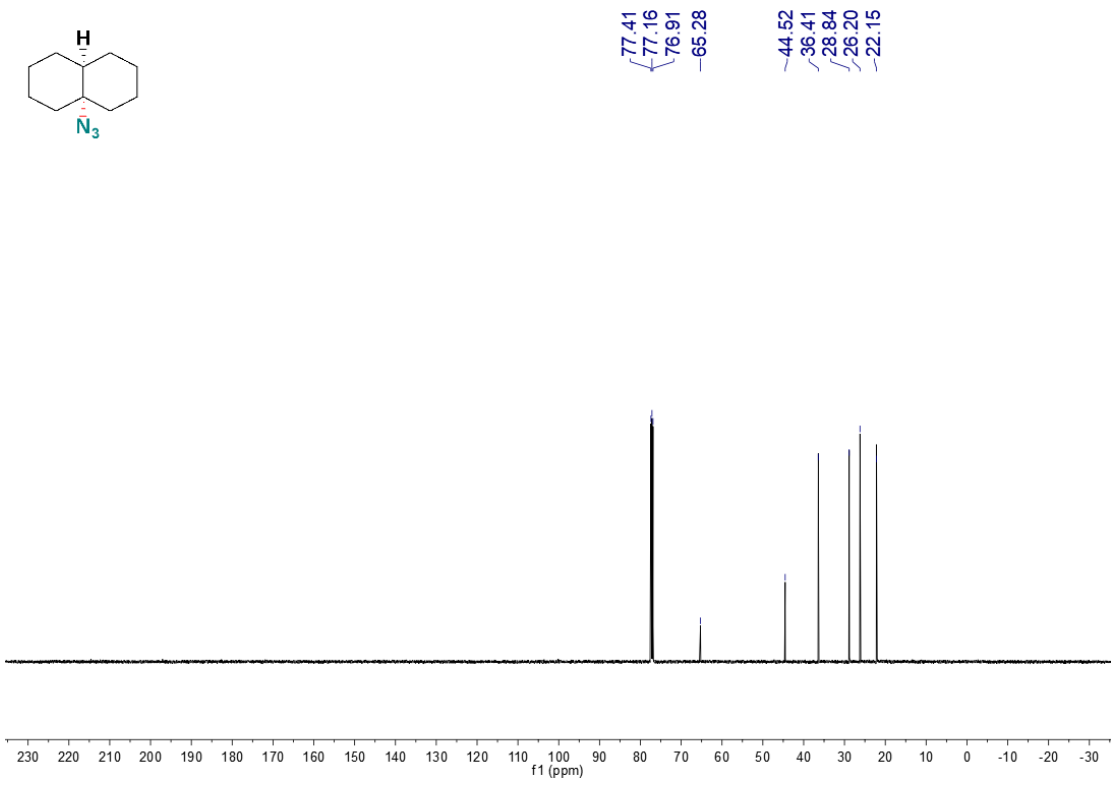
^{1}H NMR of compound **21b** (500 MHz, $CDCl_3$)



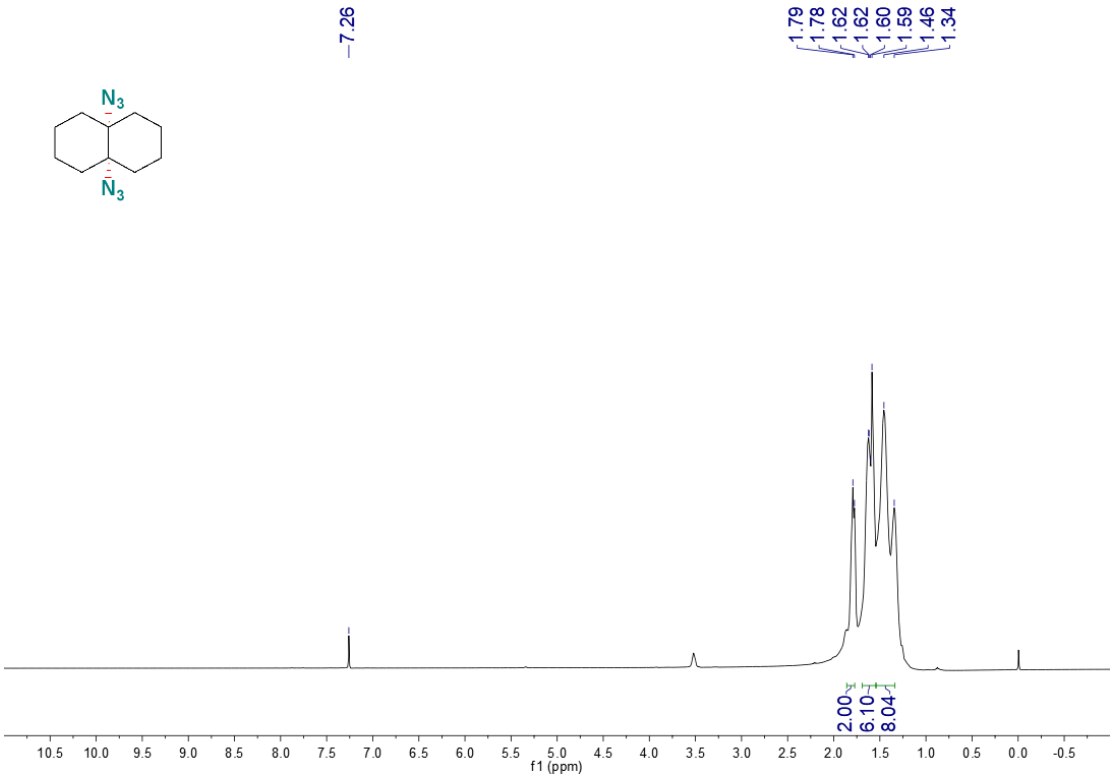
^{13}C NMR of compound **21b** (126 MHz, $CDCl_3$)



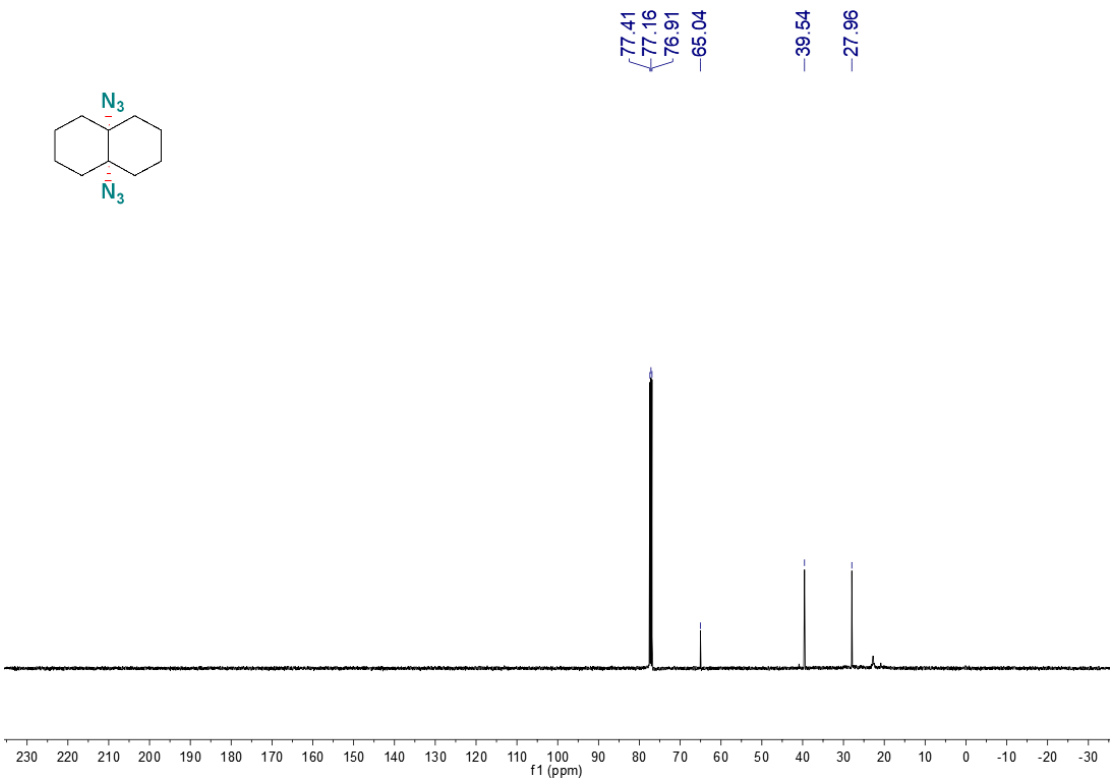
^{1}H NMR of compound **22b** (500 MHz, $CDCl_3$)



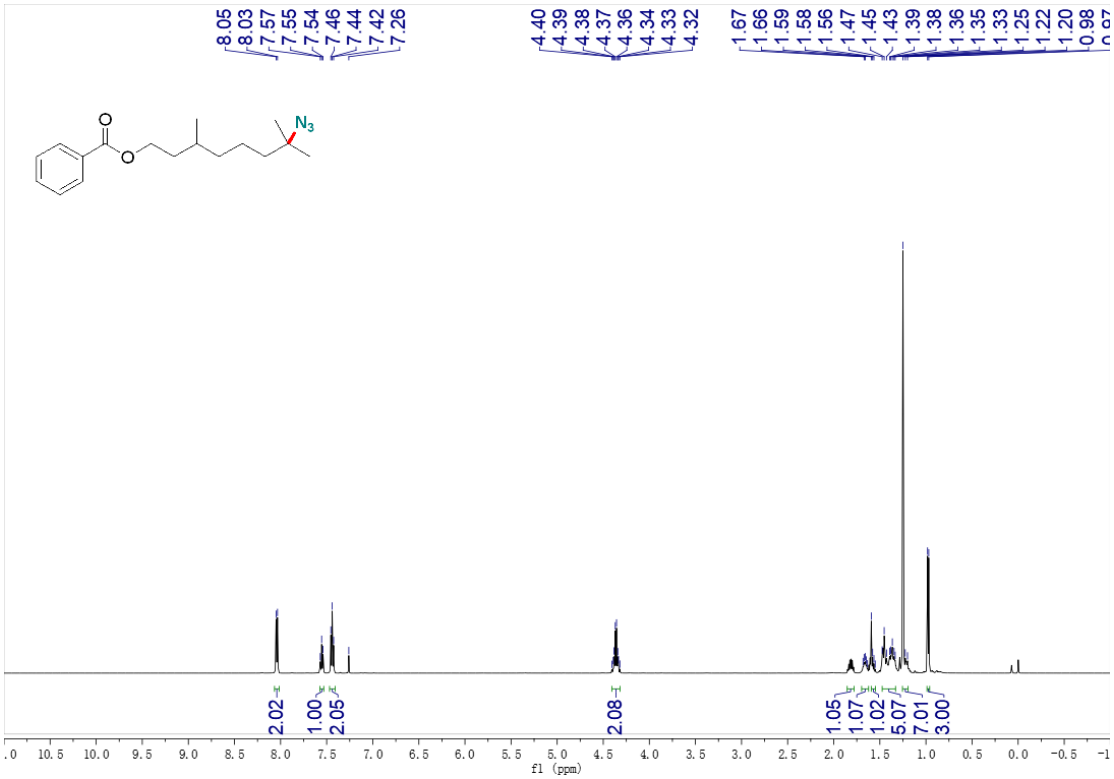
^{13}C NMR of compound **22b** (126 MHz, $CDCl_3$)



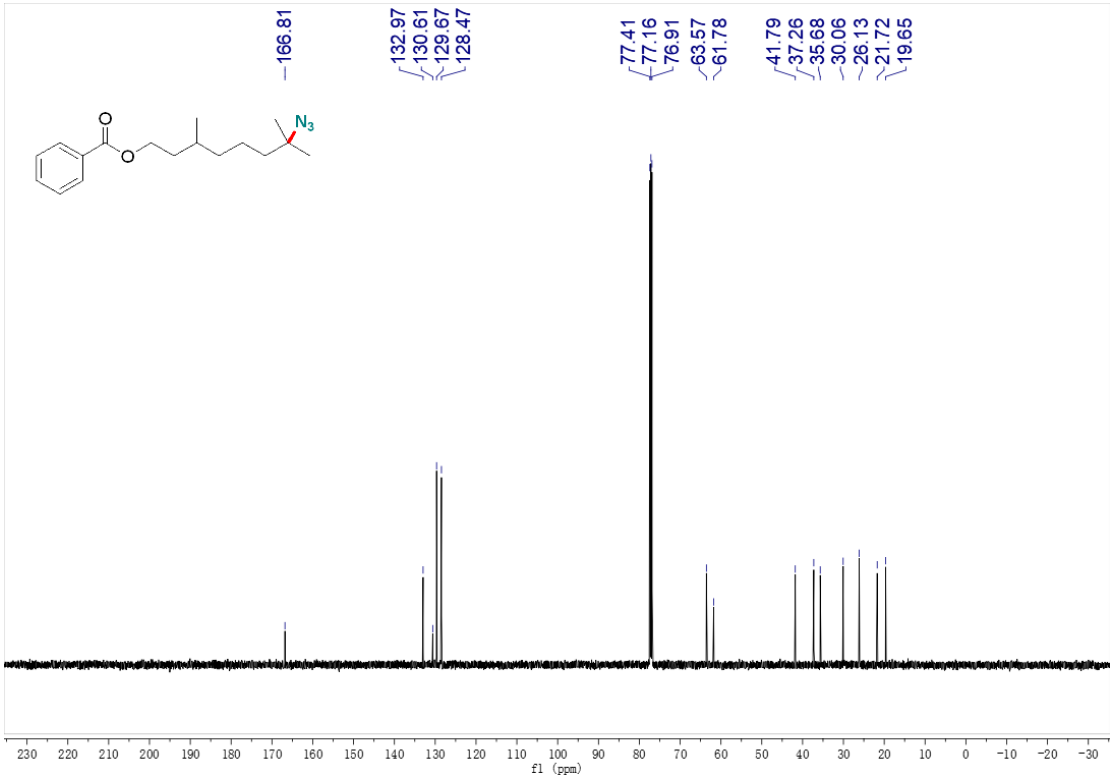
^{1}H NMR of compound **22b'** (500 MHz, $CDCl_3$)



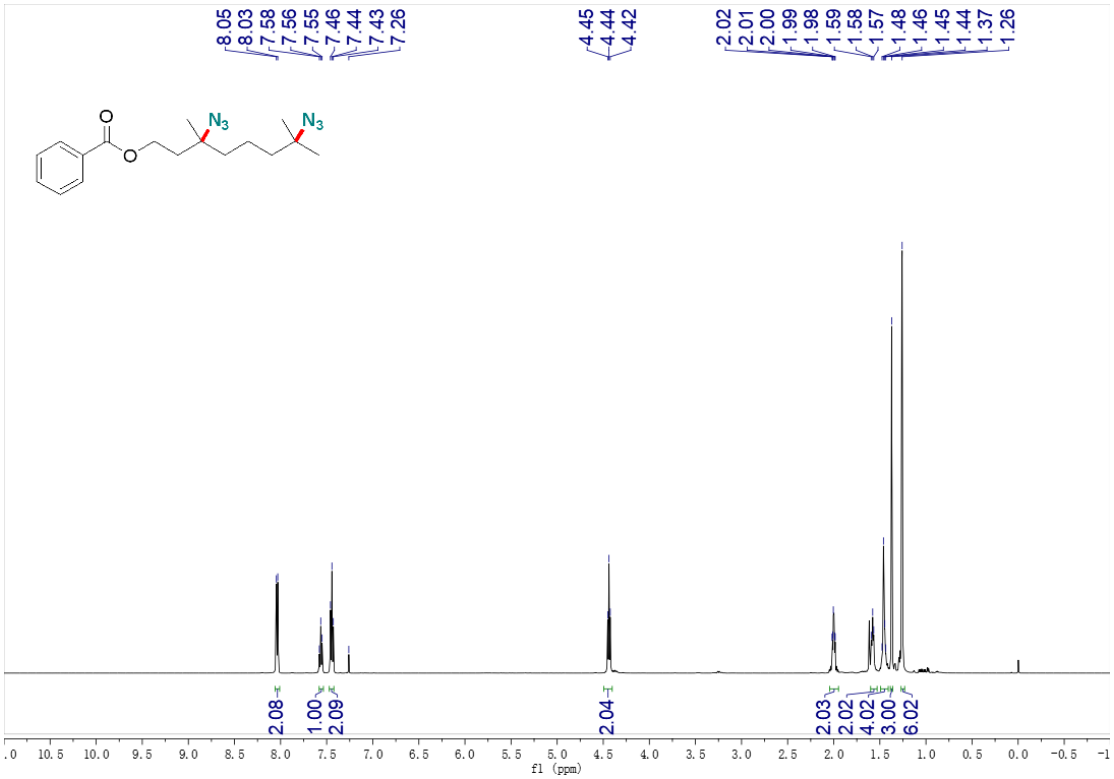
^{13}C NMR of compound **22b'** (126 MHz, $CDCl_3$)



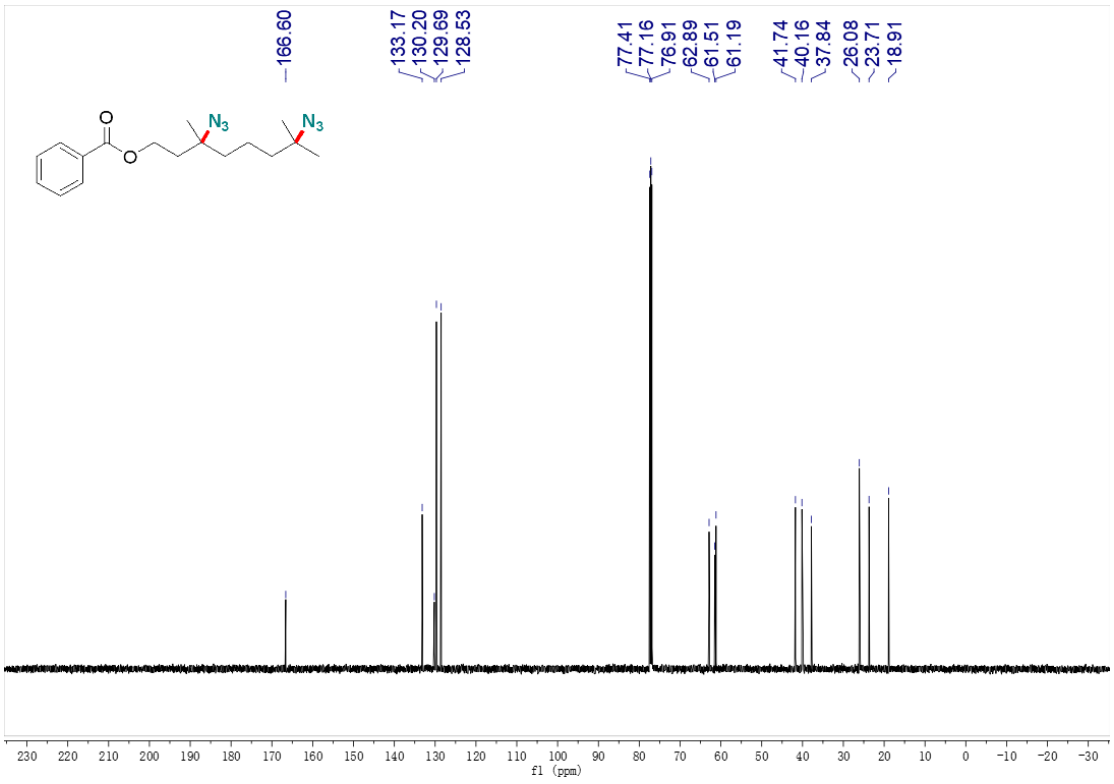
^{1}H NMR of compound **23b** (500 MHz, $CDCl_3$)



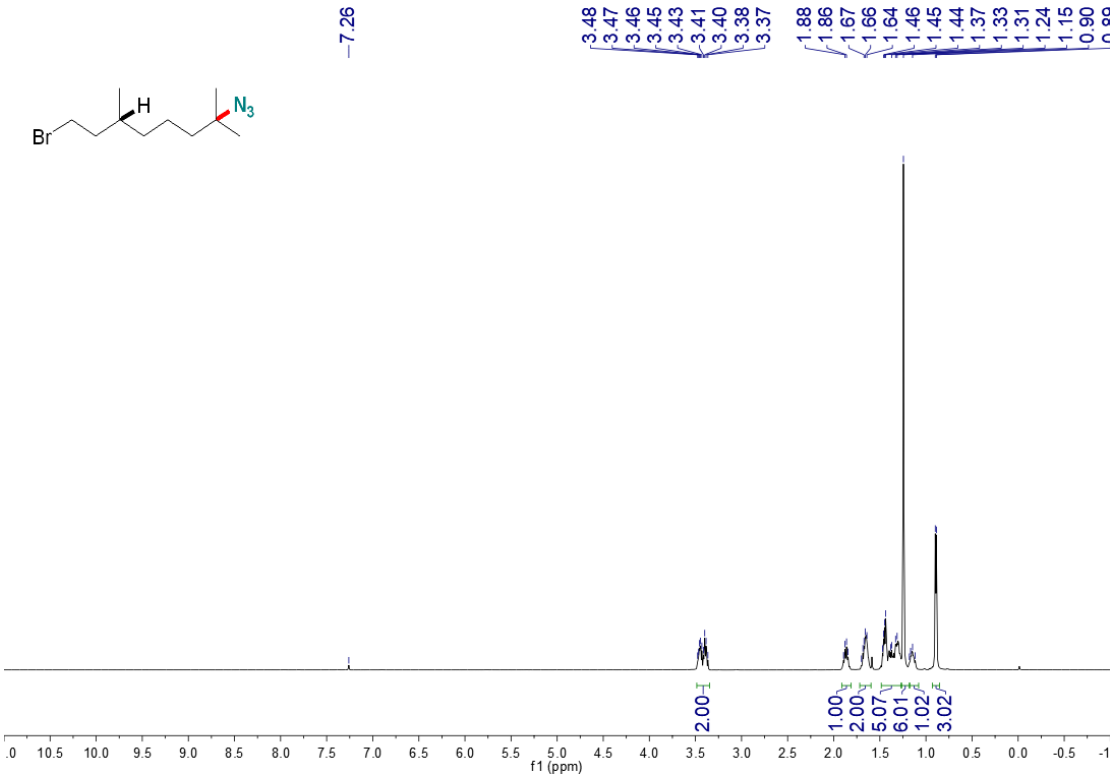
^{13}C NMR of compound **23b** (126 MHz, $CDCl_3$)



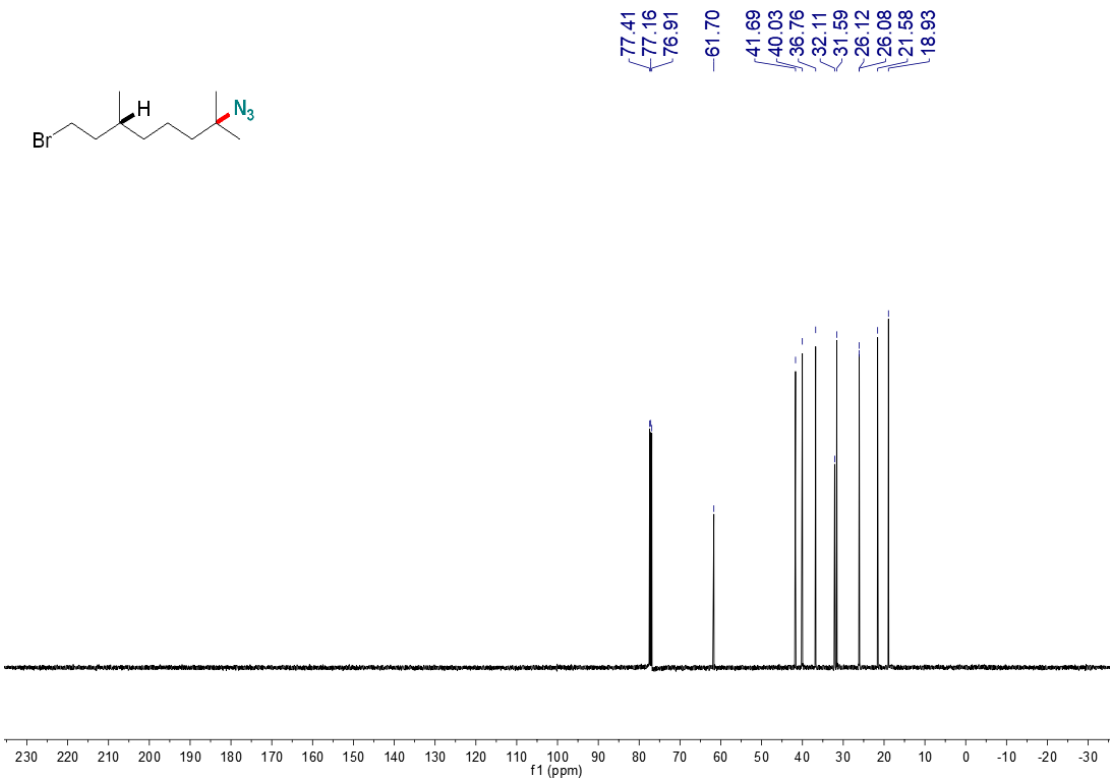
^{1}H NMR of compound **23b'** (500 MHz, $CDCl_3$)



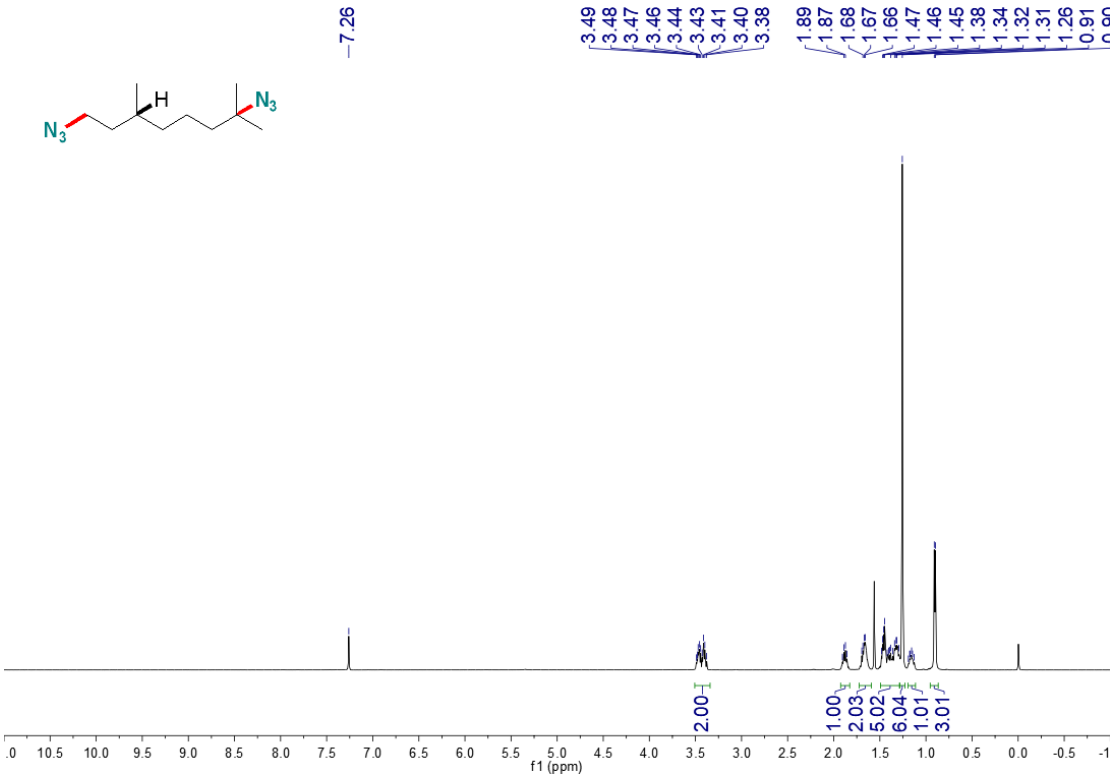
^{13}C NMR of compound **23b'** (126 MHz, $CDCl_3$)



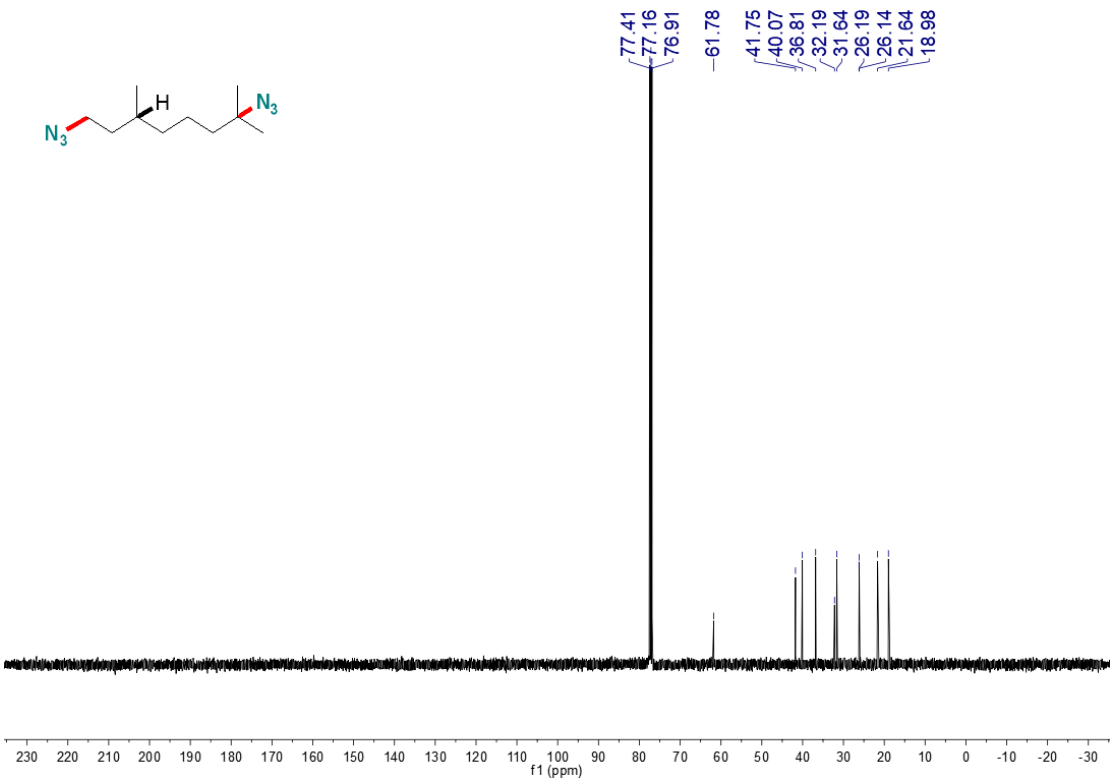
^{1}H NMR of compound **24b** (500 MHz, $CDCl_3$)



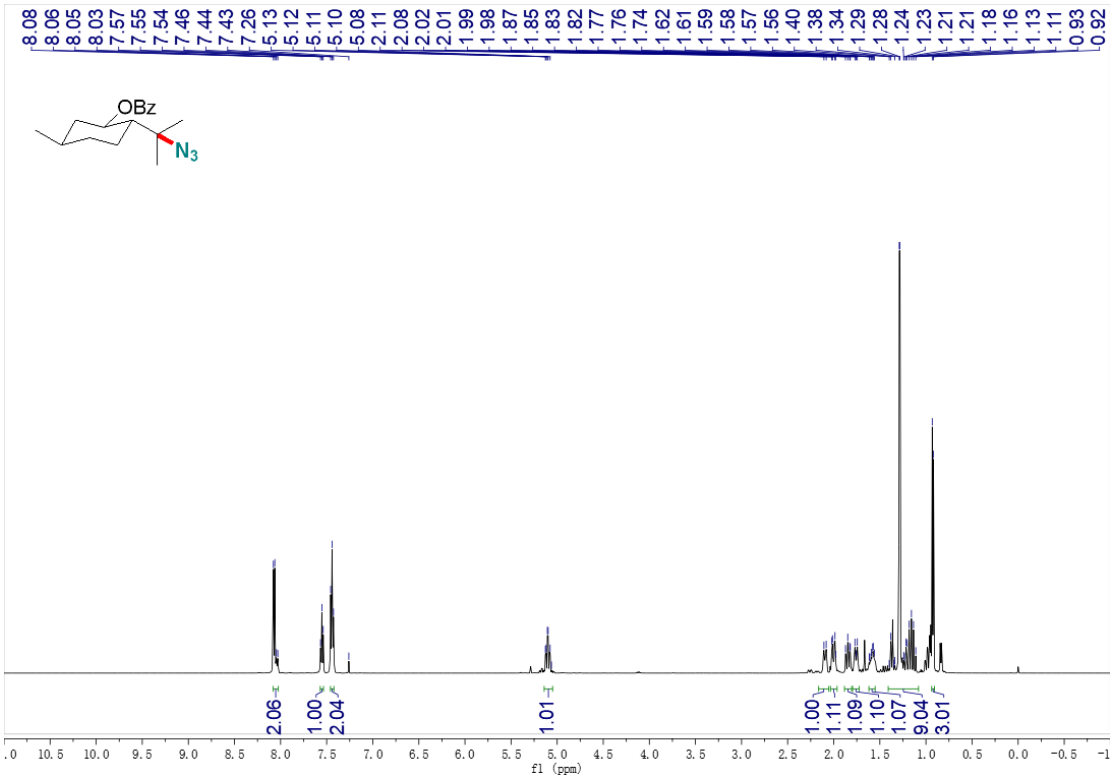
^{13}C NMR of compound **24b** (126 MHz, $CDCl_3$)



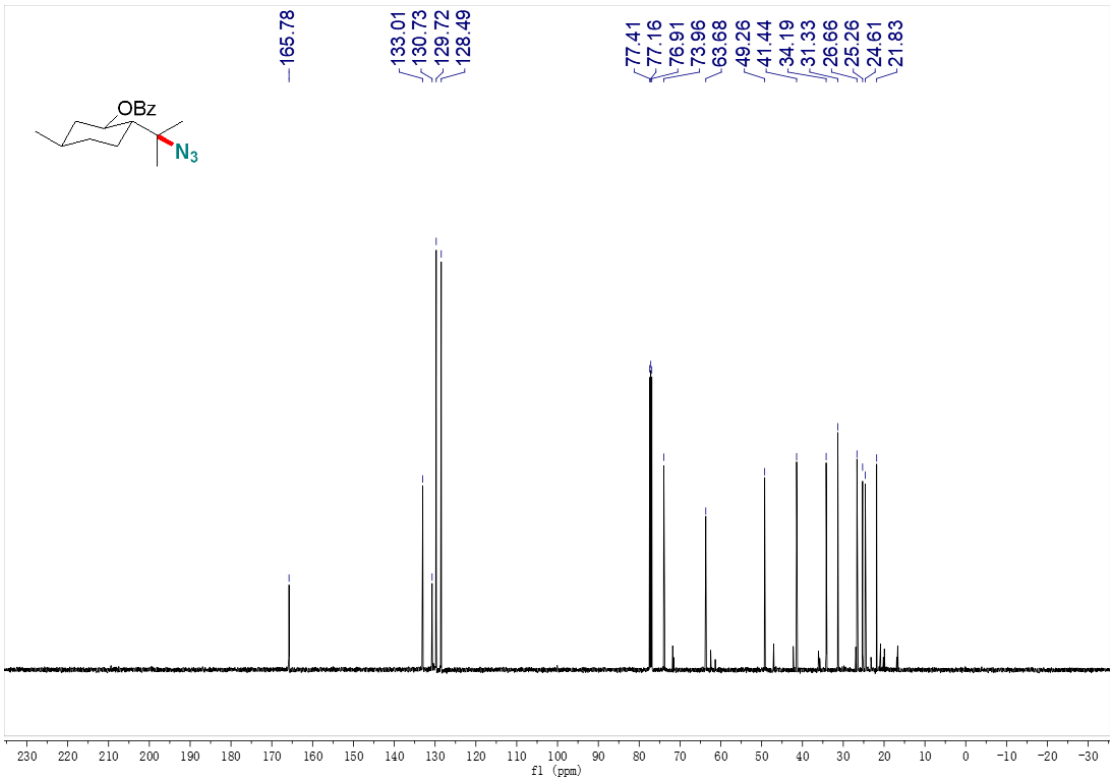
^{1}H NMR of compound **24b'** (500 MHz, $CDCl_3$)



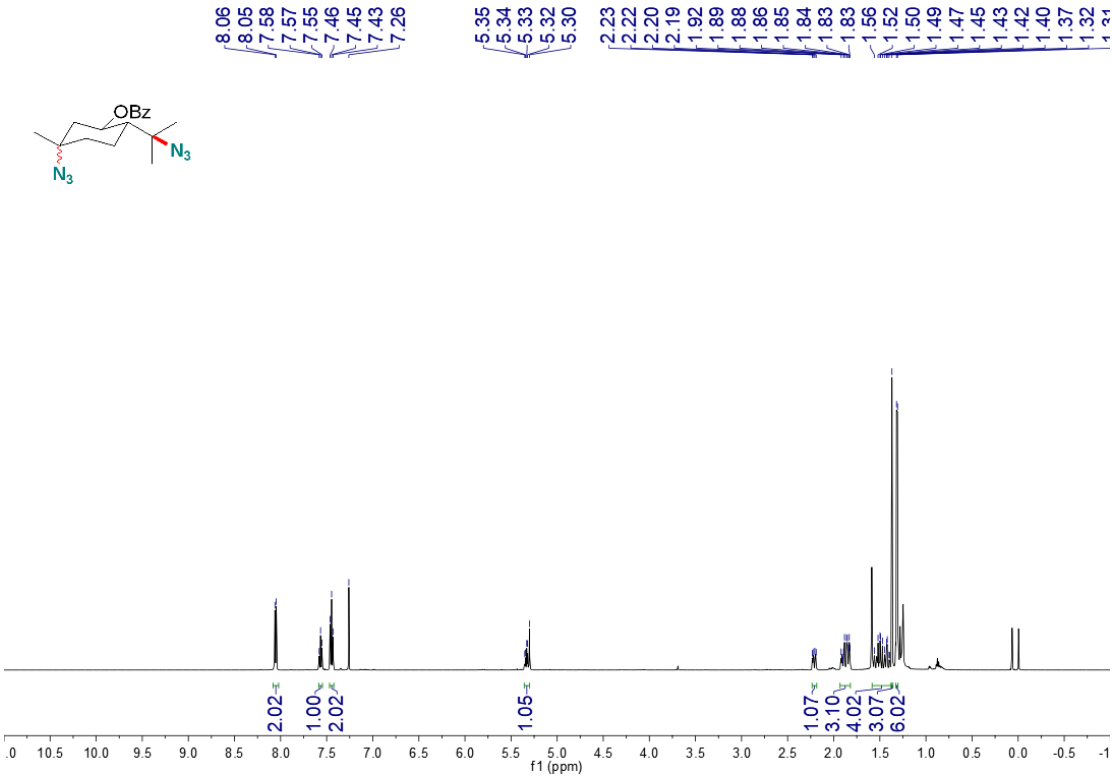
^{13}C NMR of compound **24b'** (126 MHz, $CDCl_3$)



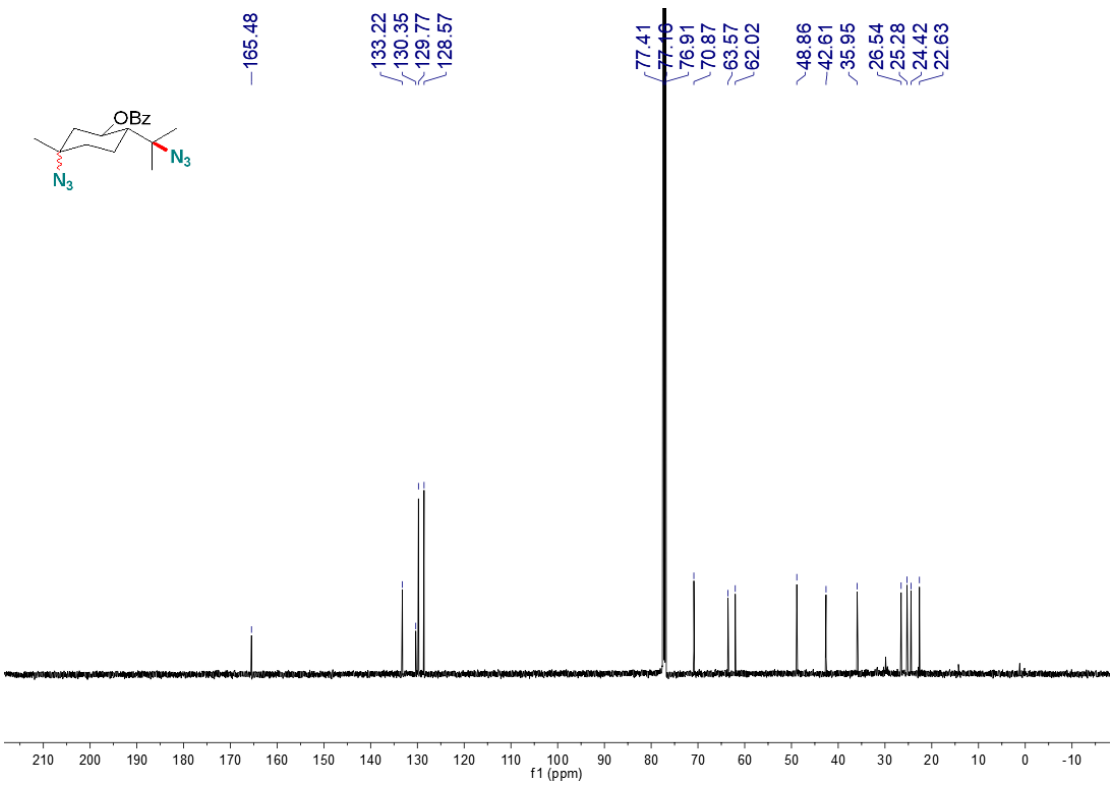
^{1}H NMR of compound **25b** (500 MHz, $CDCl_3$)



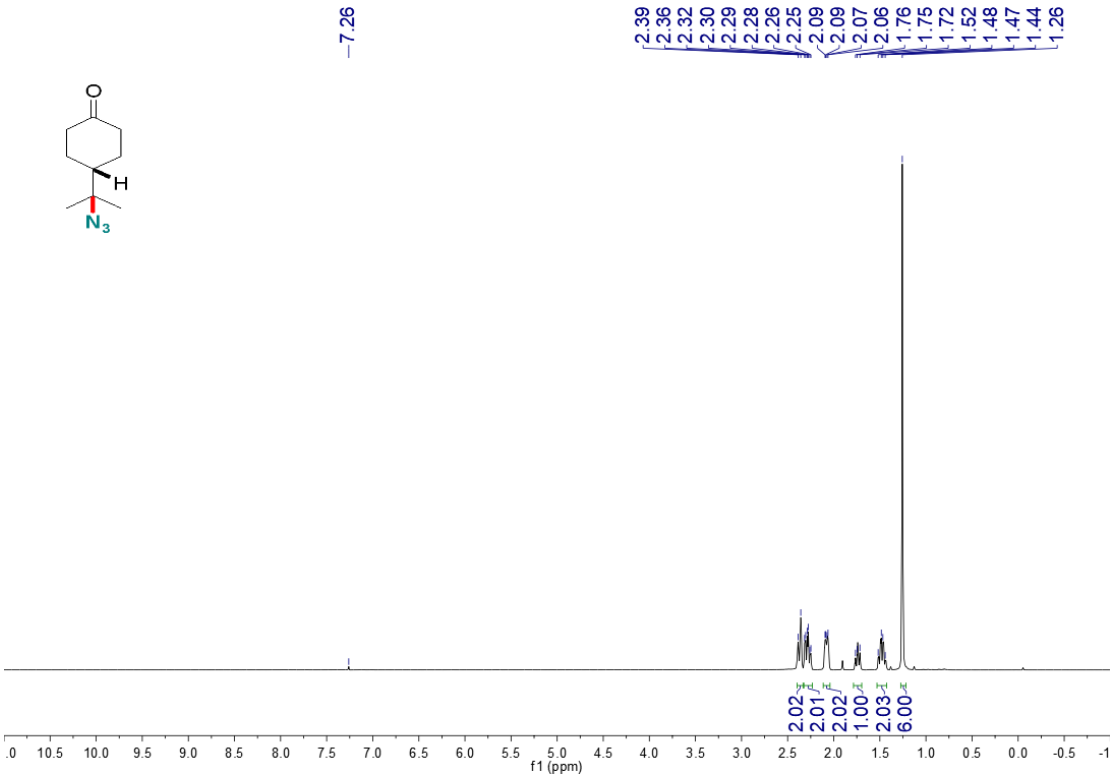
^{13}C NMR of compound **25b** (126 MHz, $CDCl_3$)



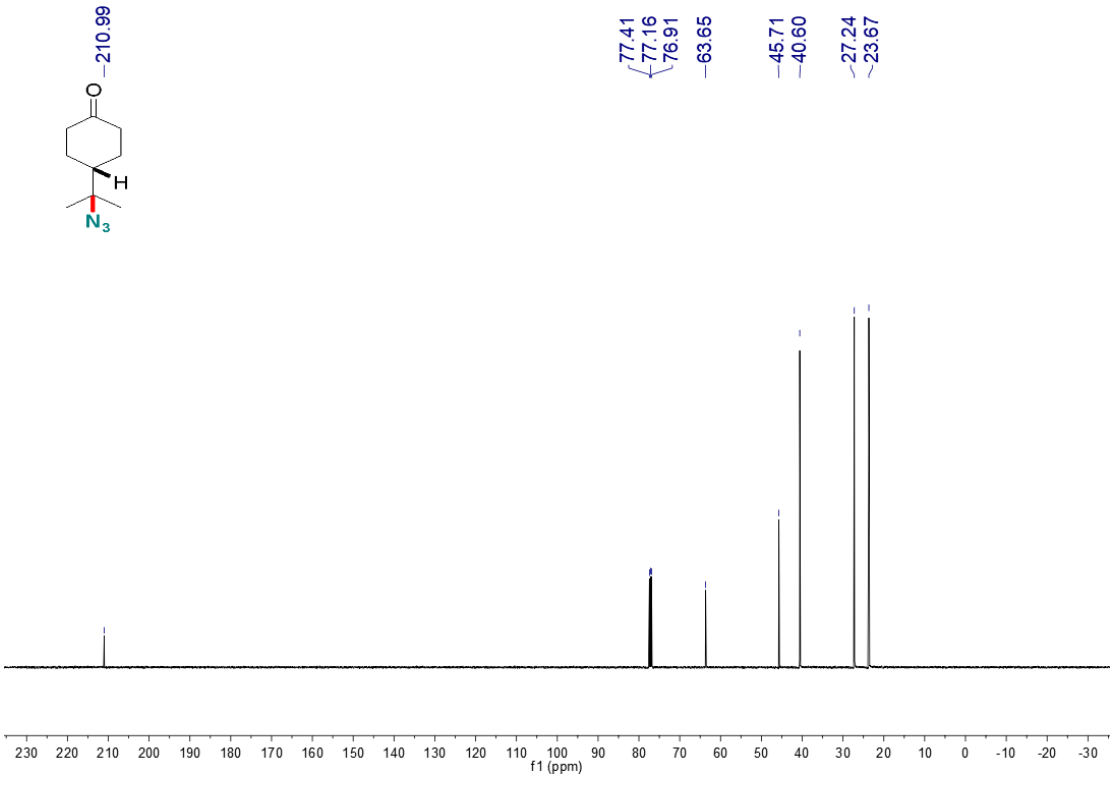
^{1}H NMR of compound **25b'** (500 MHz, $CDCl_3$)



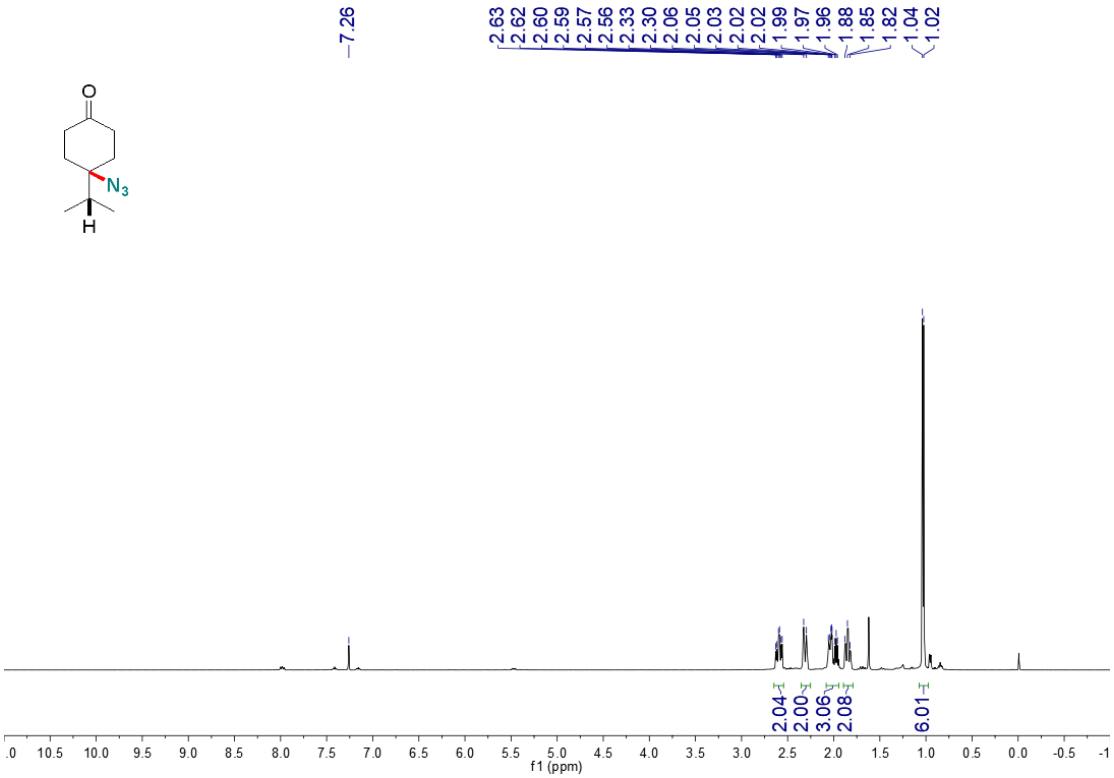
^{13}C NMR of compound **25b'** (126 MHz, $CDCl_3$)



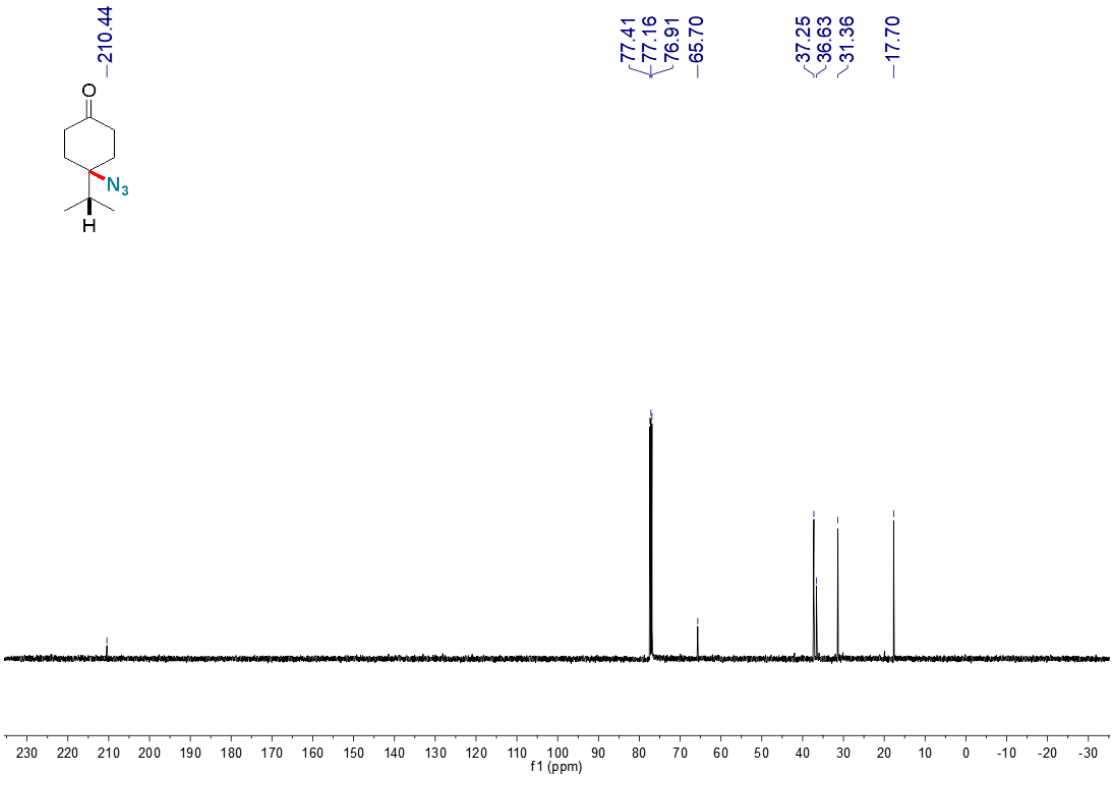
^{1}H NMR of compound **26b** (500 MHz, $CDCl_3$)



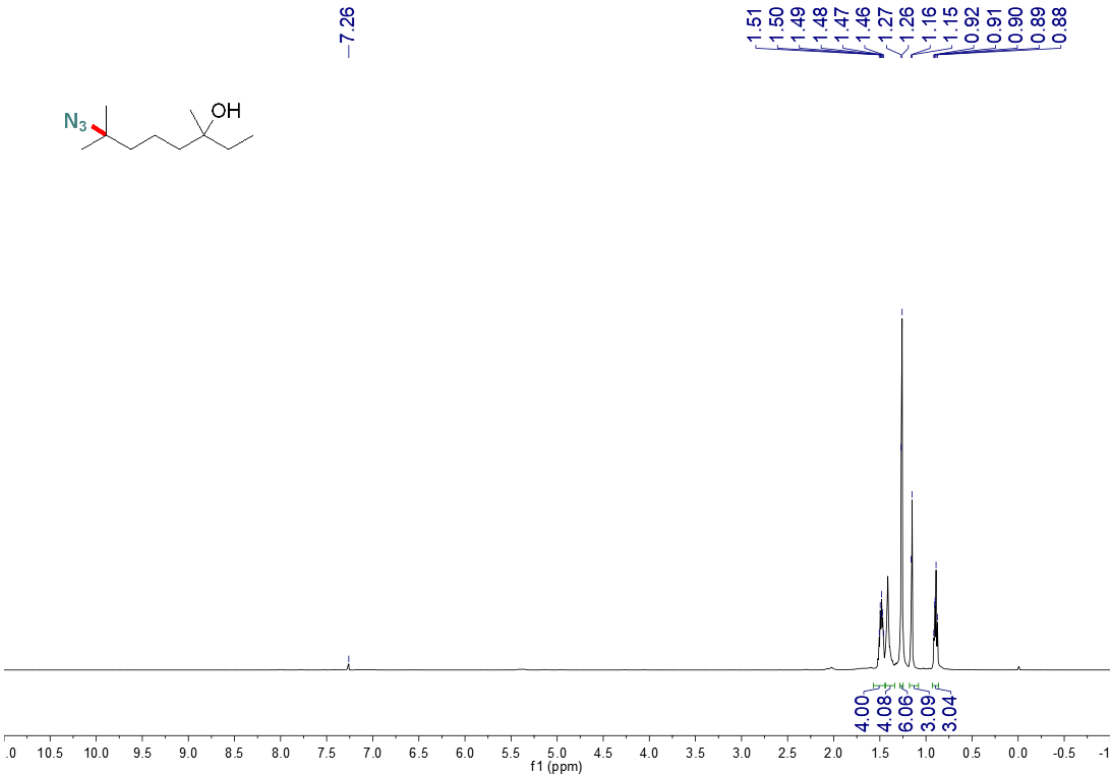
^{13}C NMR of compound **26b** (126 MHz, $CDCl_3$)



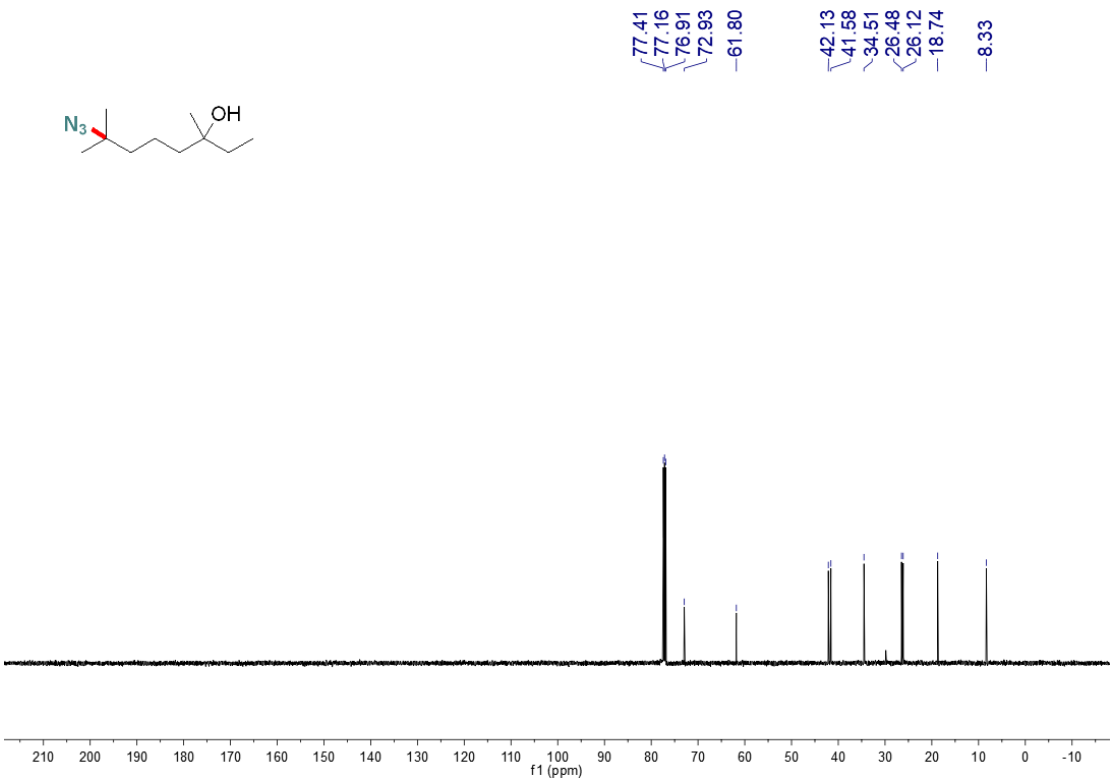
^{1}H NMR of compound **26b'** (500 MHz, $CDCl_3$)



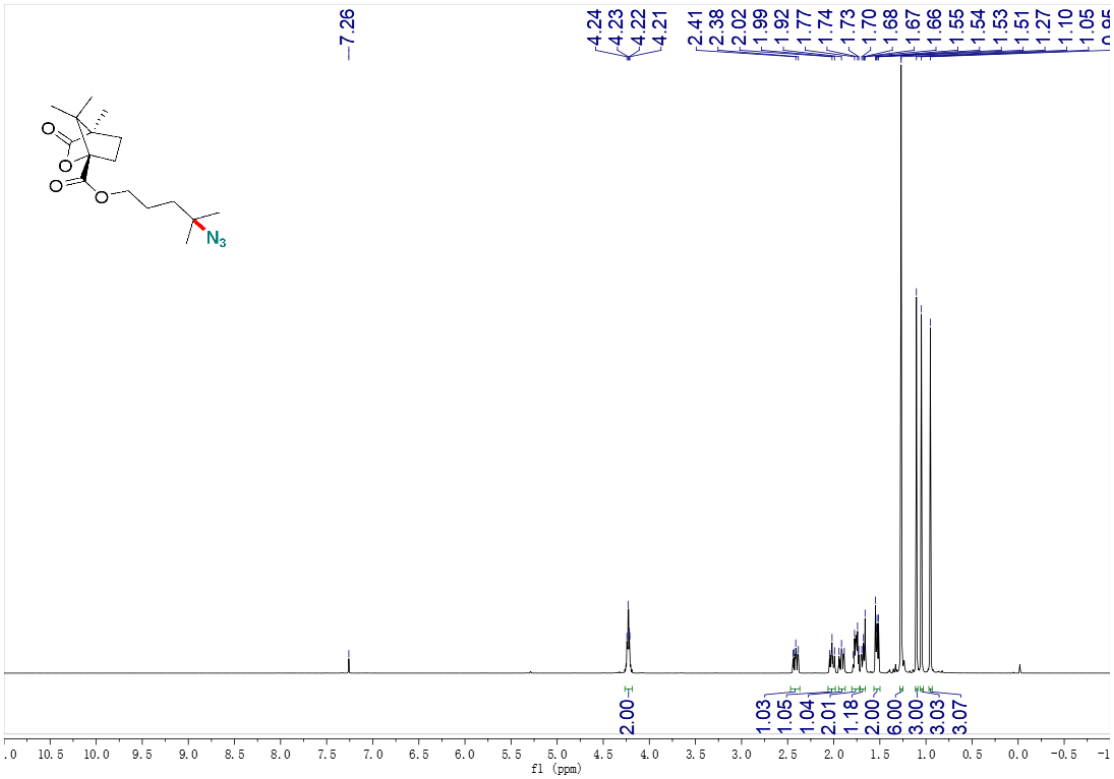
^{13}C NMR of compound **26b'** (126 MHz, $CDCl_3$)



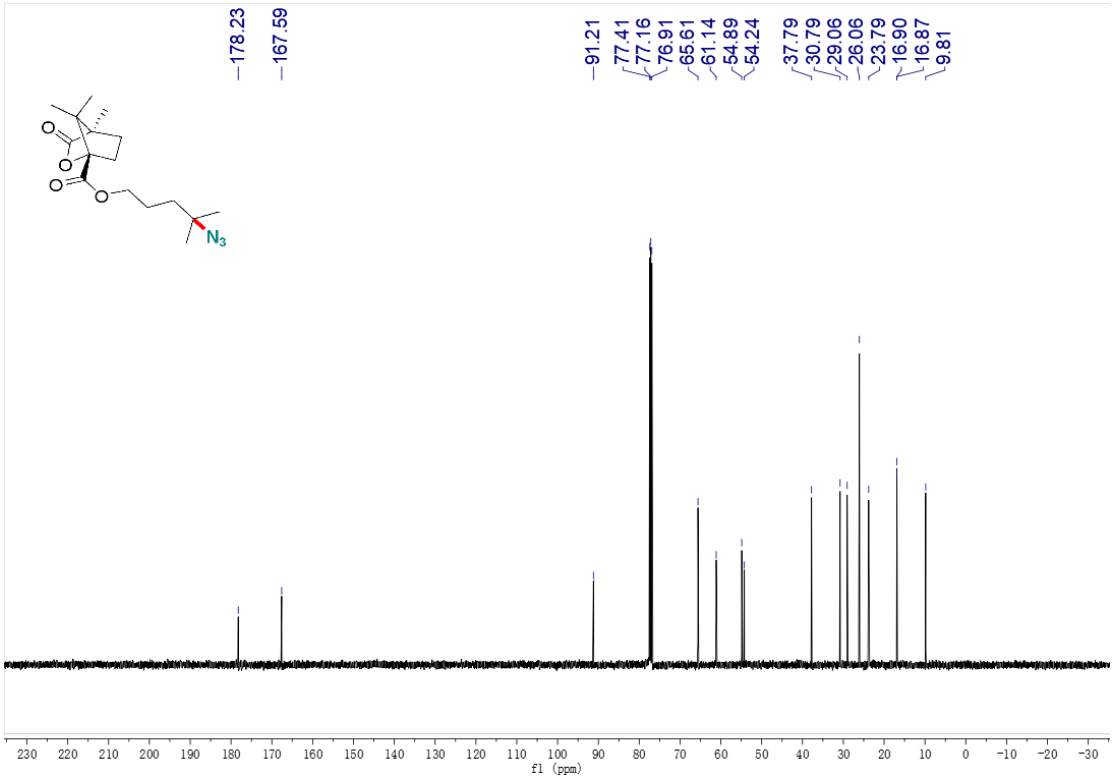
^{1}H NMR of compound **27b** (500 MHz, $CDCl_3$)



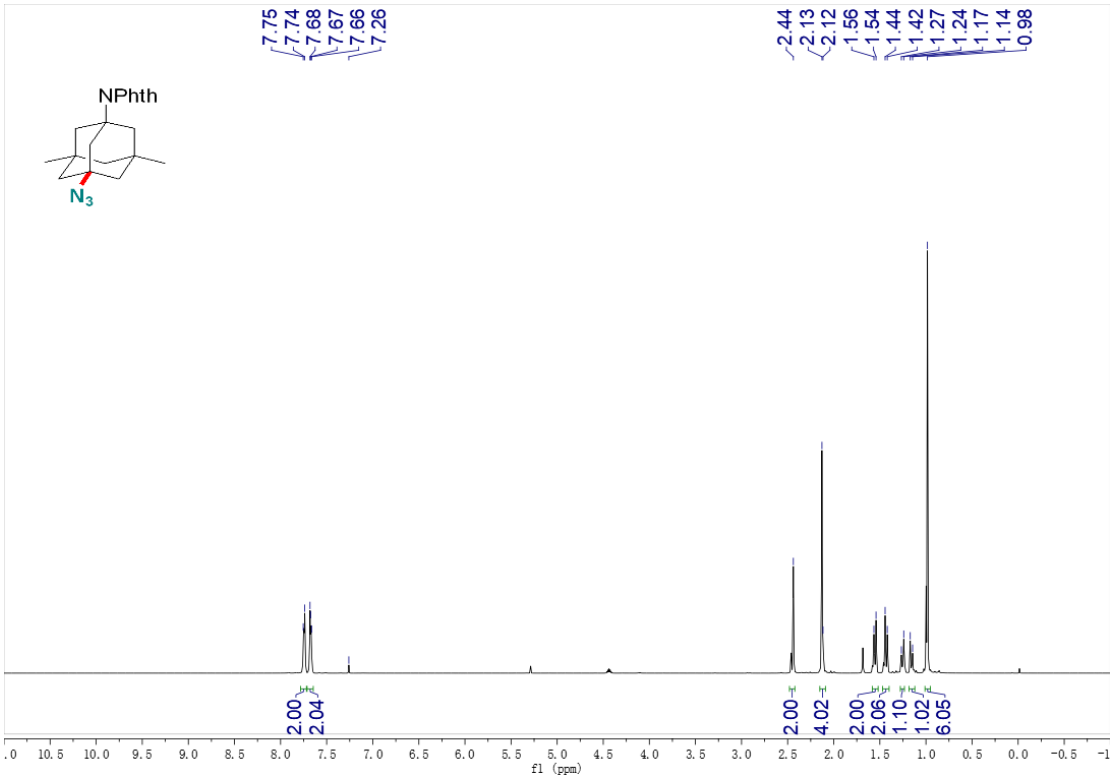
^{13}C NMR of compound **27b** (126 MHz, $CDCl_3$)



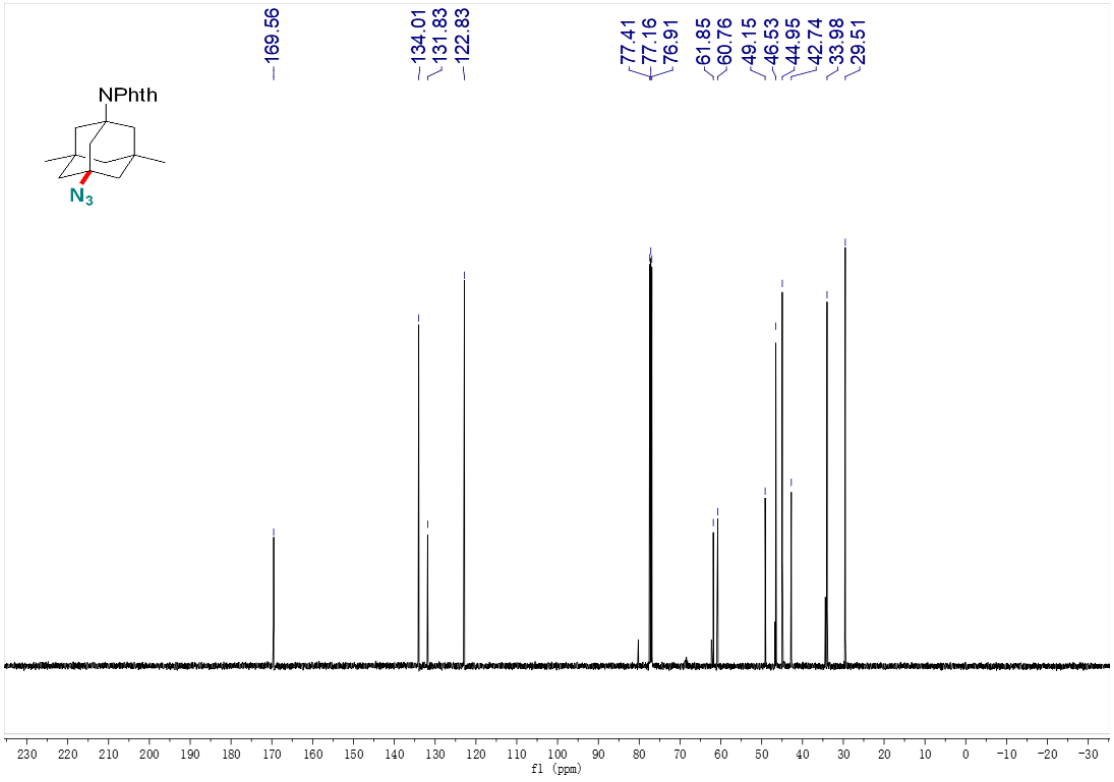
^{1}H NMR of compound **28b** (500 MHz, $CDCl_3$)



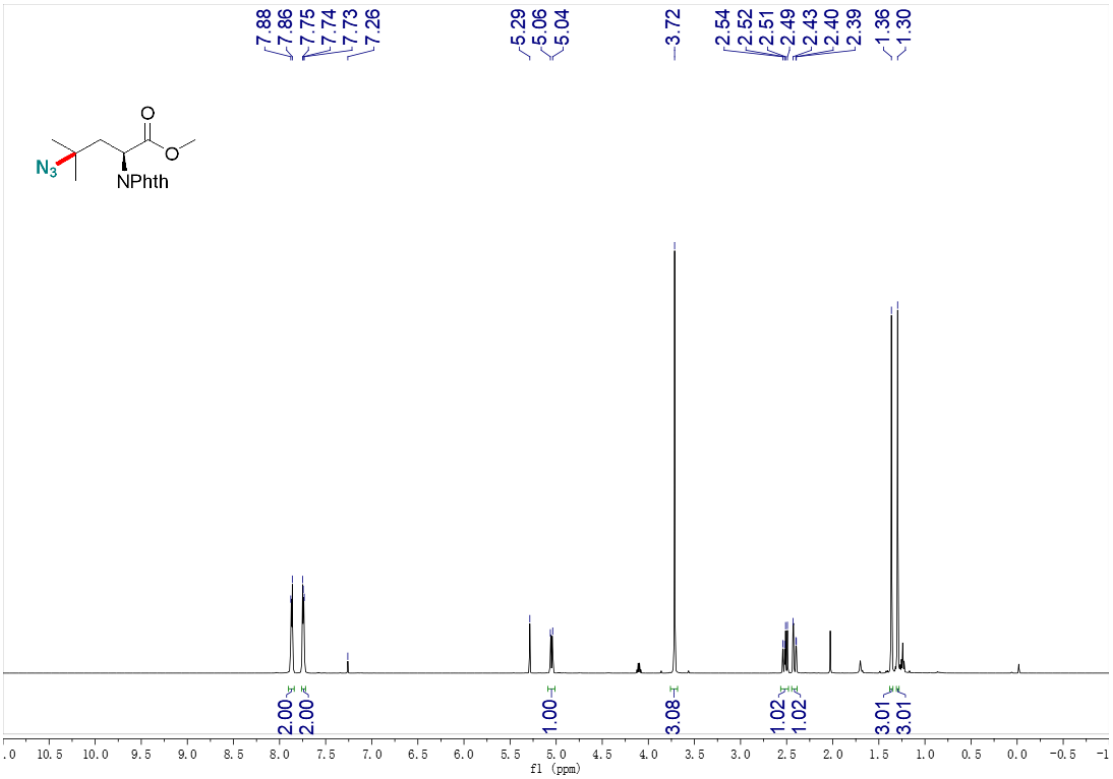
^{13}C NMR of compound **28b** (126 MHz, $CDCl_3$)



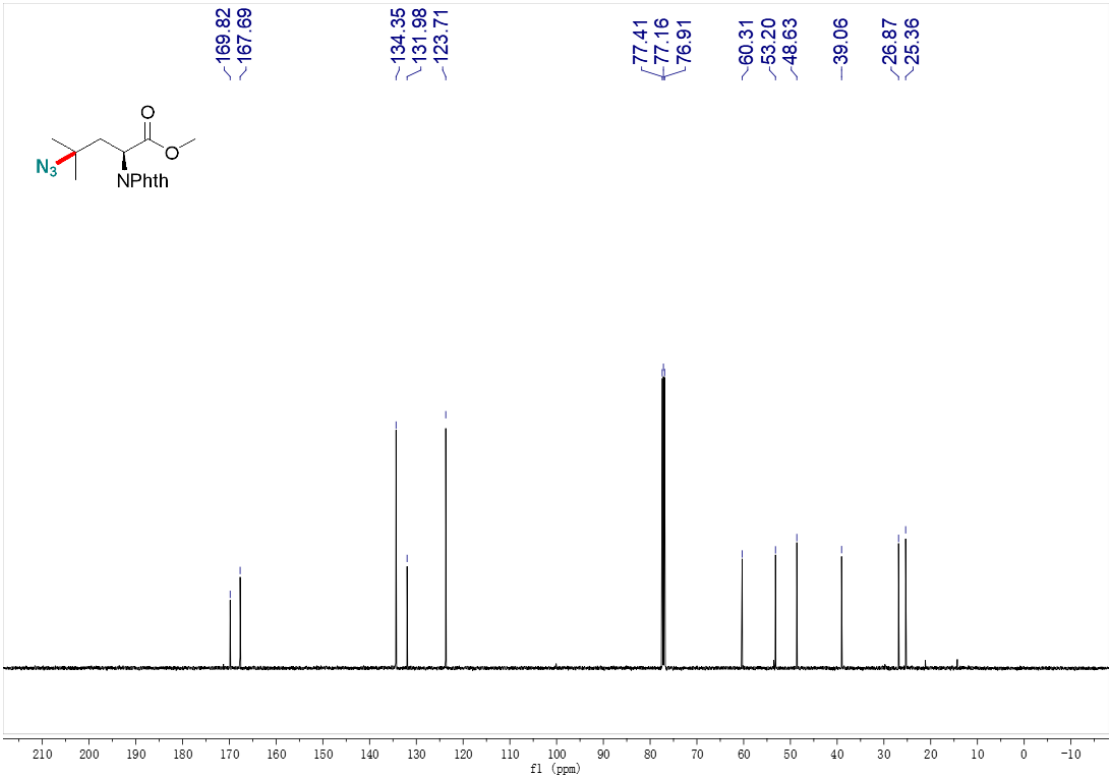
^{1}H NMR of compound **29b** (500 MHz, $CDCl_3$)



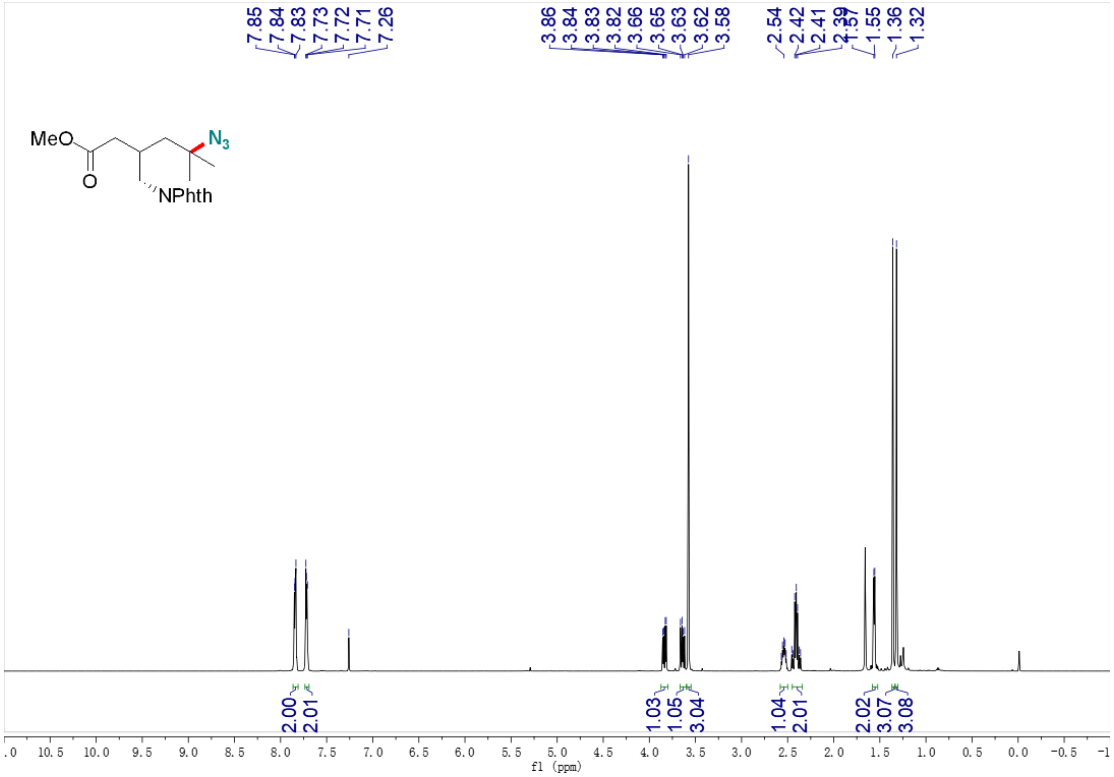
^{13}C NMR of compound **29b** (126 MHz, $CDCl_3$)



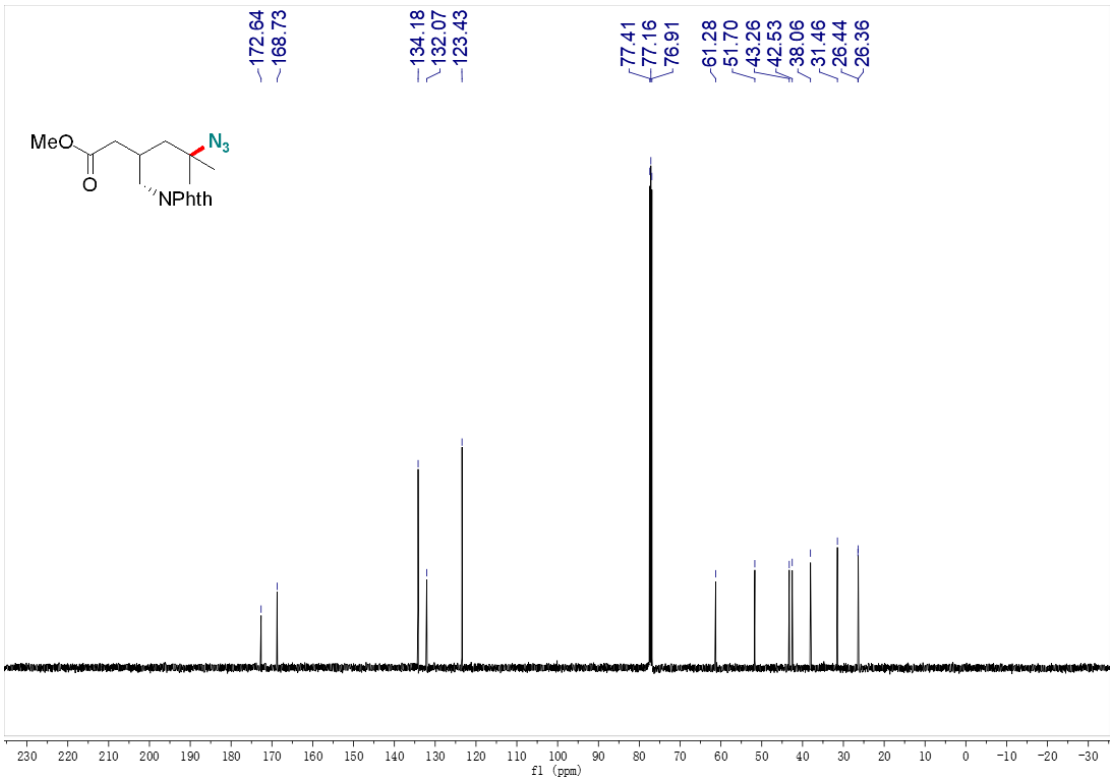
^{1}H NMR of compound **30b** (500 MHz, $CDCl_3$)



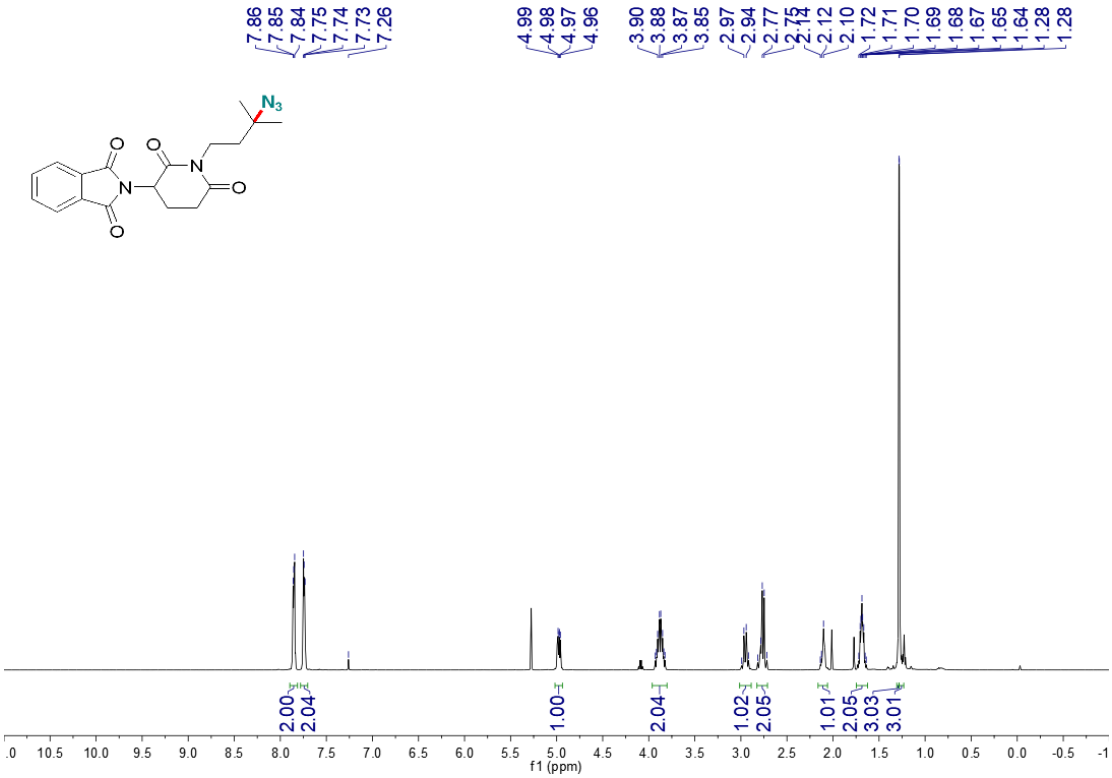
^{13}C NMR of compound **30b** (126 MHz, $CDCl_3$)



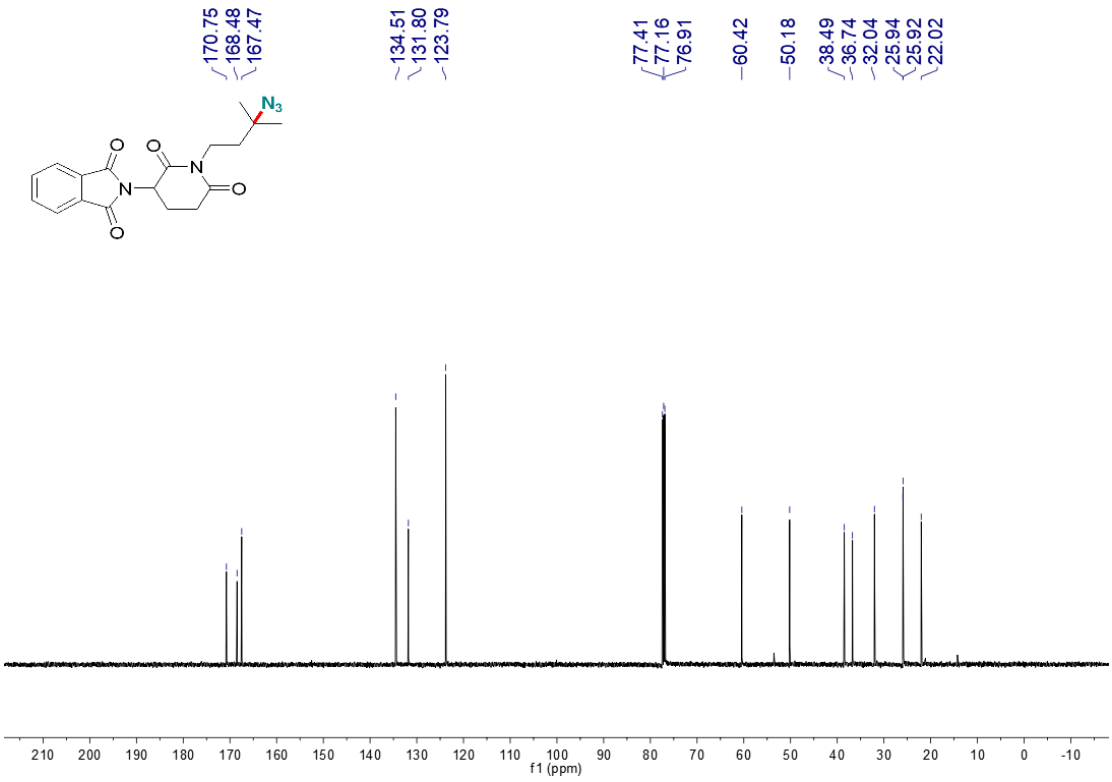
^{1}H NMR of compound **31b** (500 MHz, $CDCl_3$)



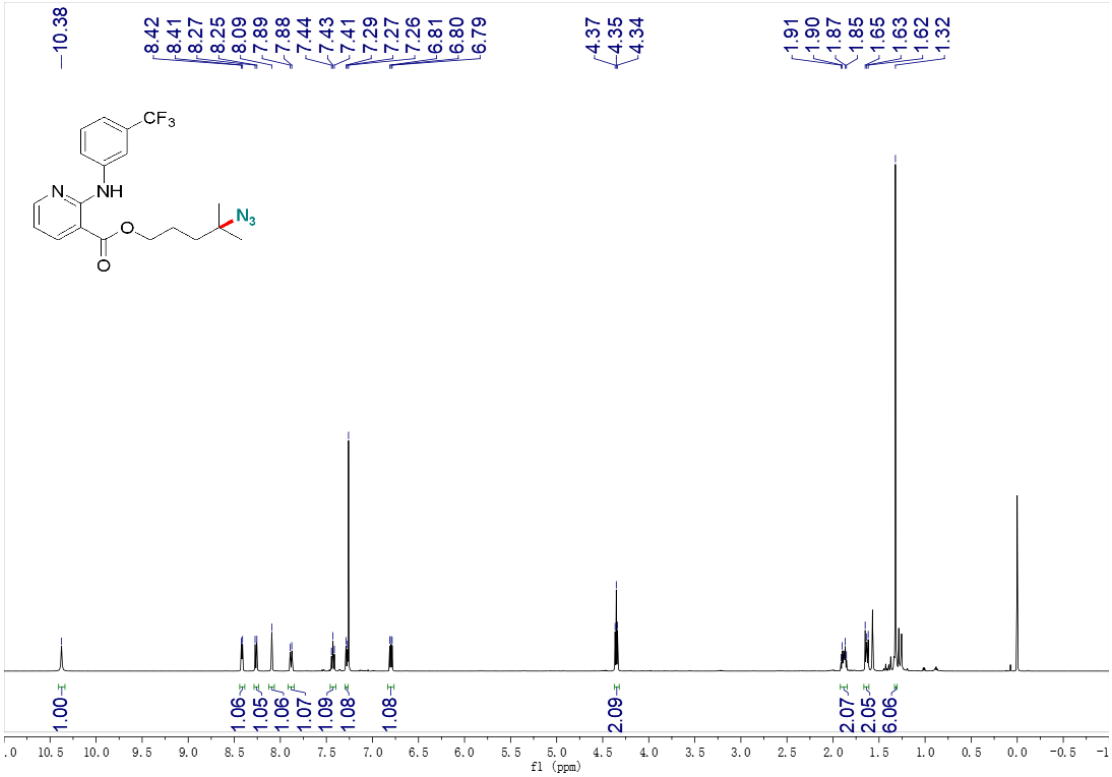
^{13}C NMR of compound **31b** (126 MHz, $CDCl_3$)



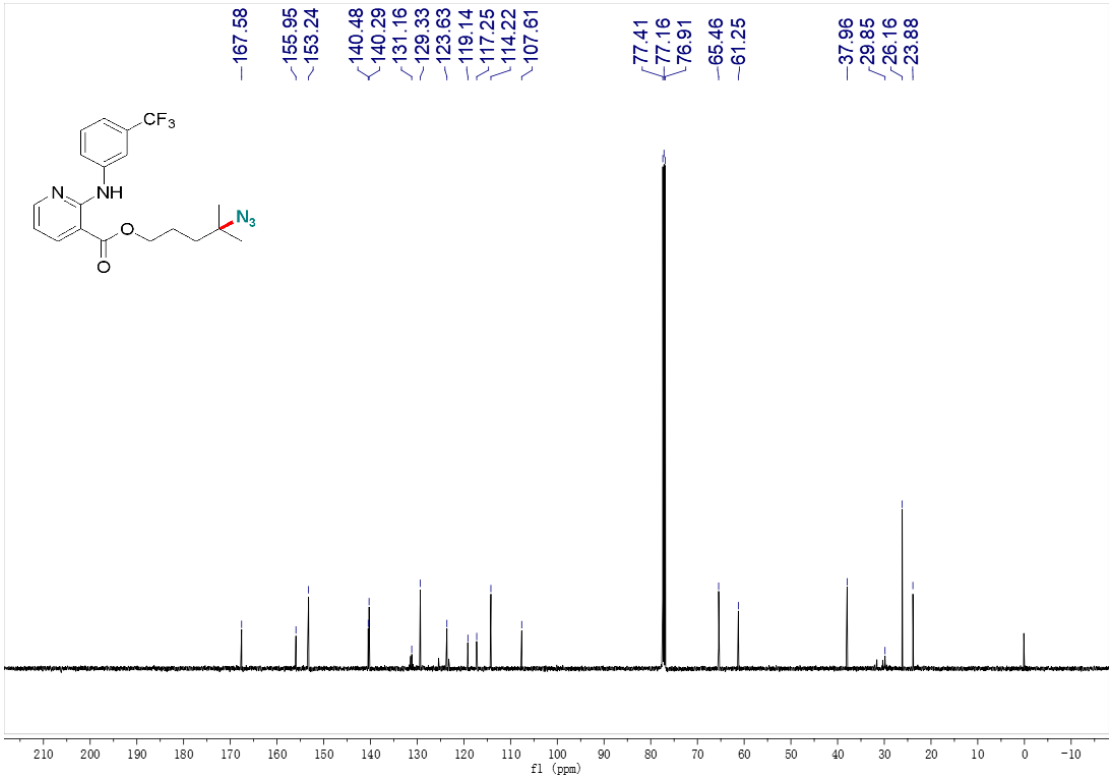
^{1}H NMR of compound **32b** (500 MHz, $CDCl_3$)



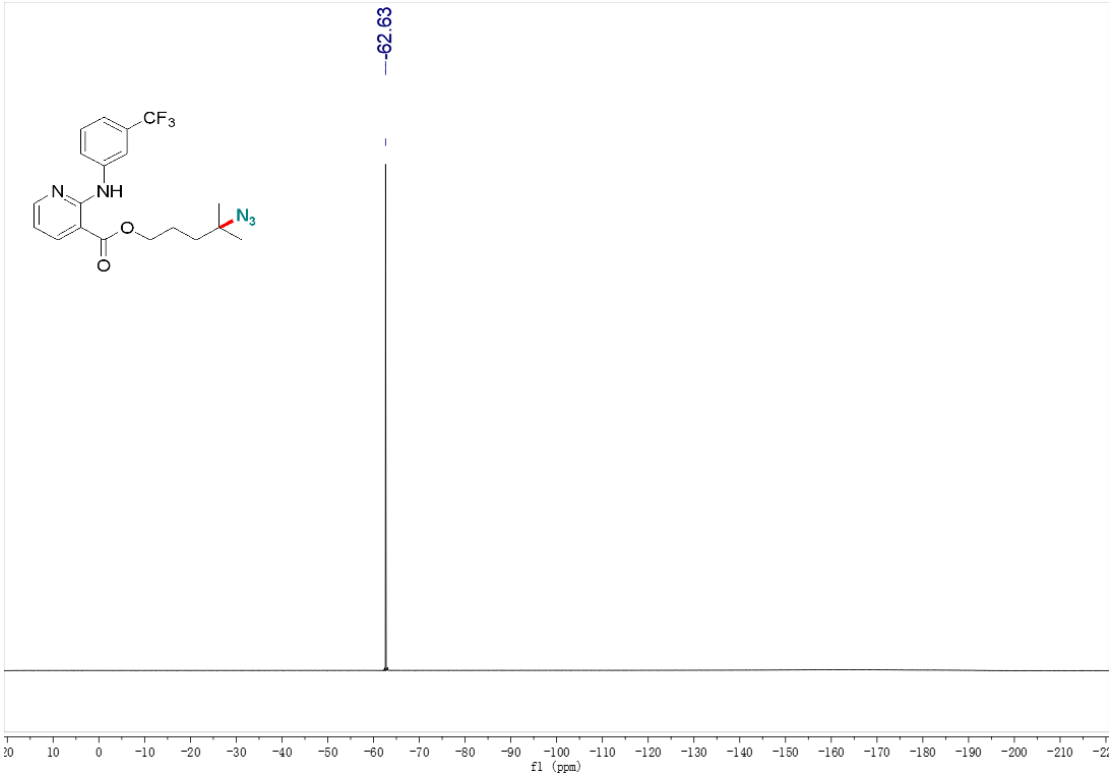
^{13}C NMR of compound **32b** (126 MHz, $CDCl_3$)



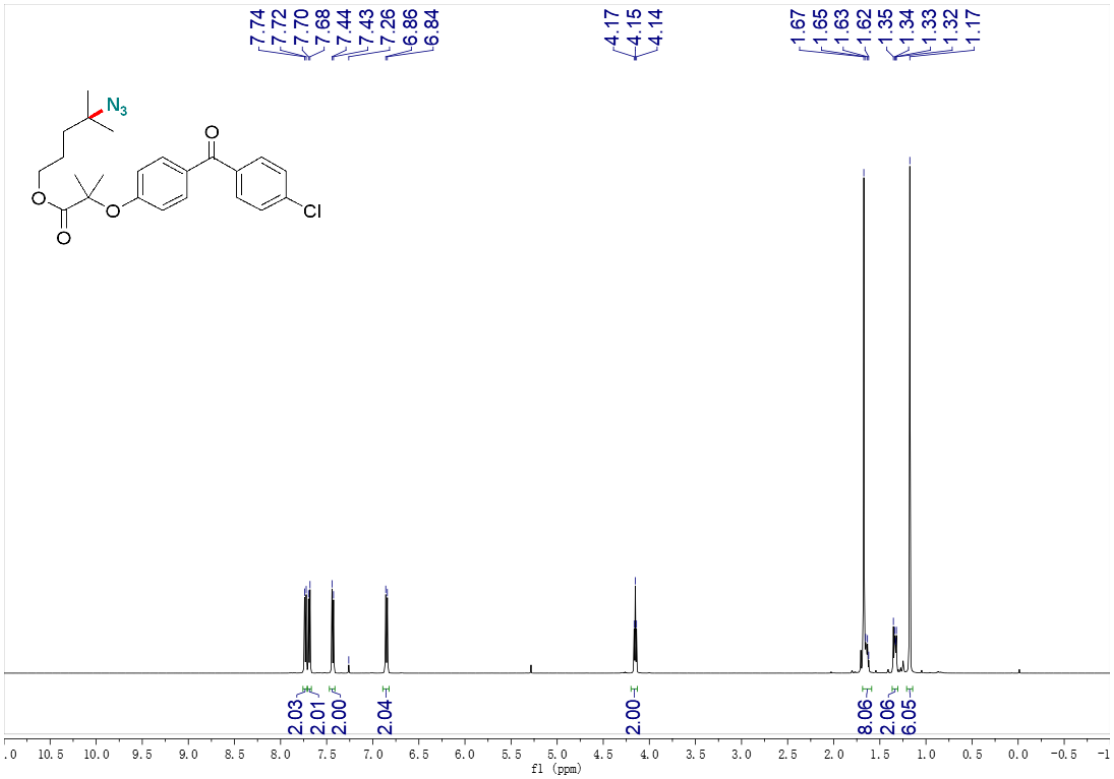
^{1}H NMR of compound **33b** (500 MHz, $CDCl_3$)



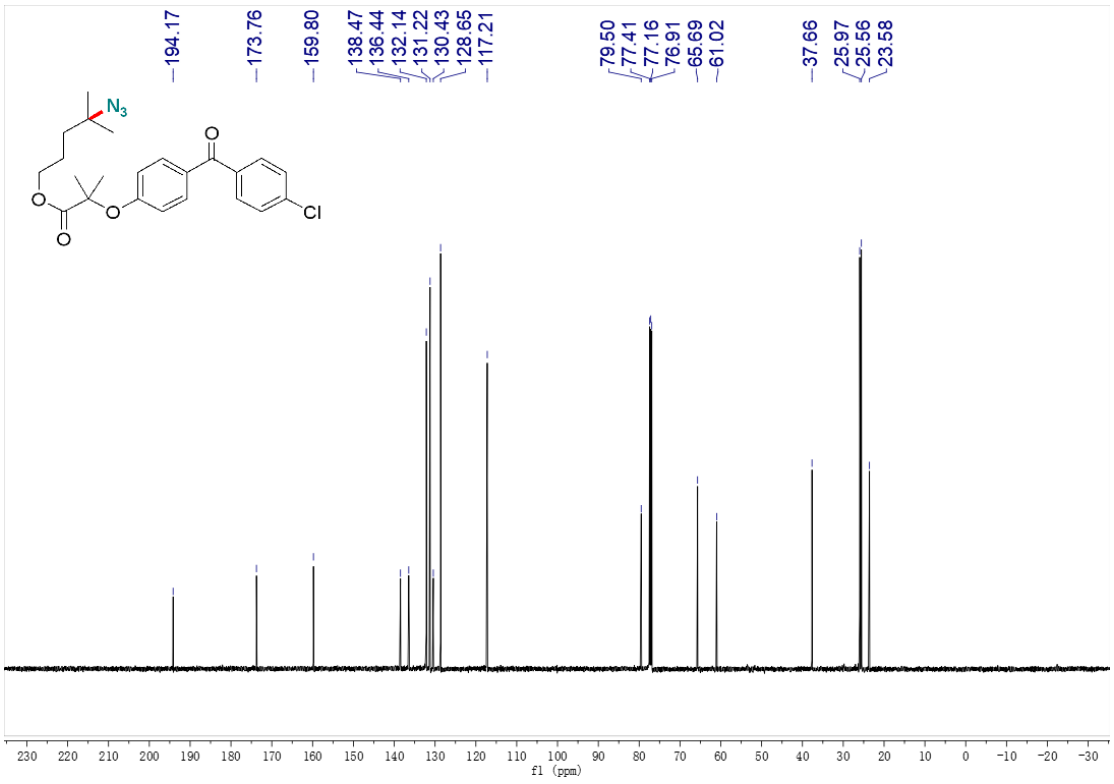
^{13}C NMR of compound **33b** (126 MHz, $CDCl_3$)



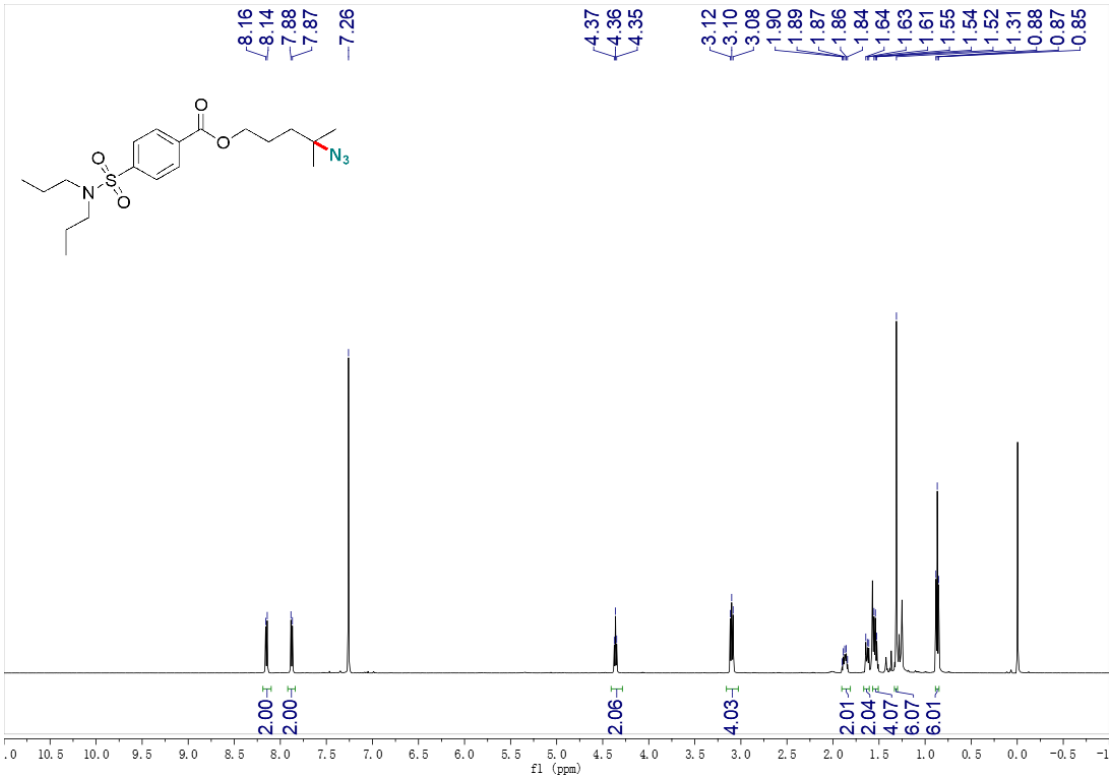
^{19}F NMR of compound **33b** (471 MHz, $CDCl_3$)



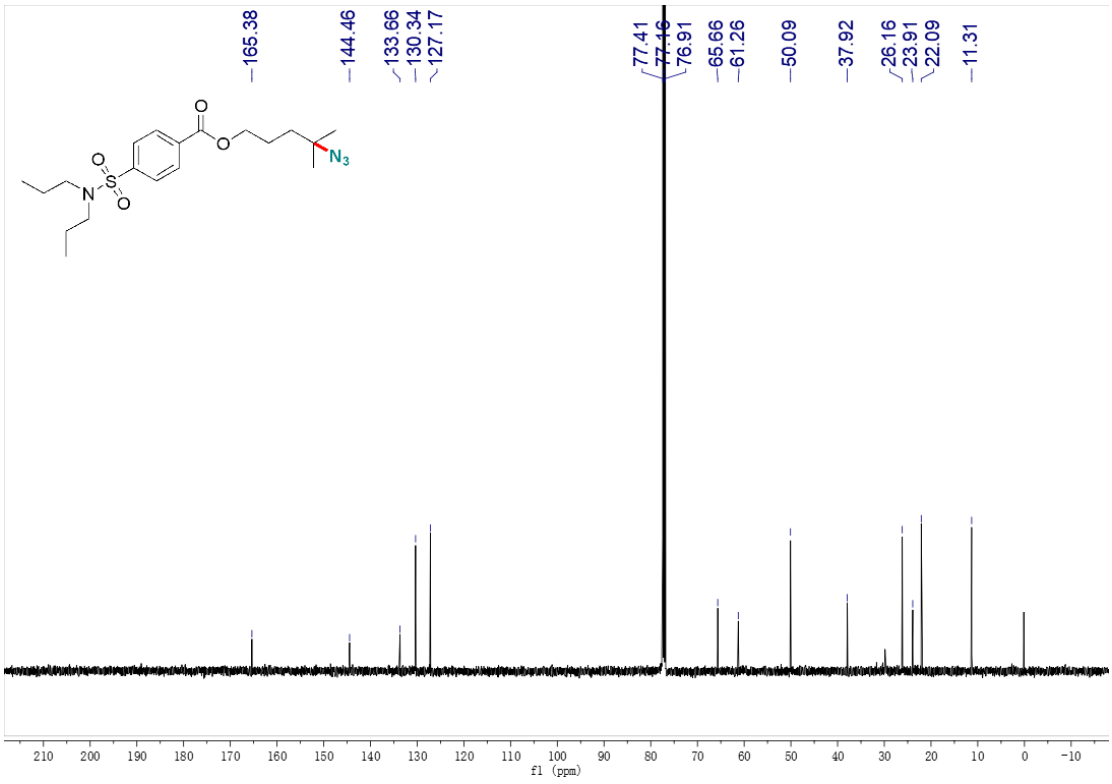
^{1}H NMR of compound **34b** (500 MHz, $CDCl_3$)



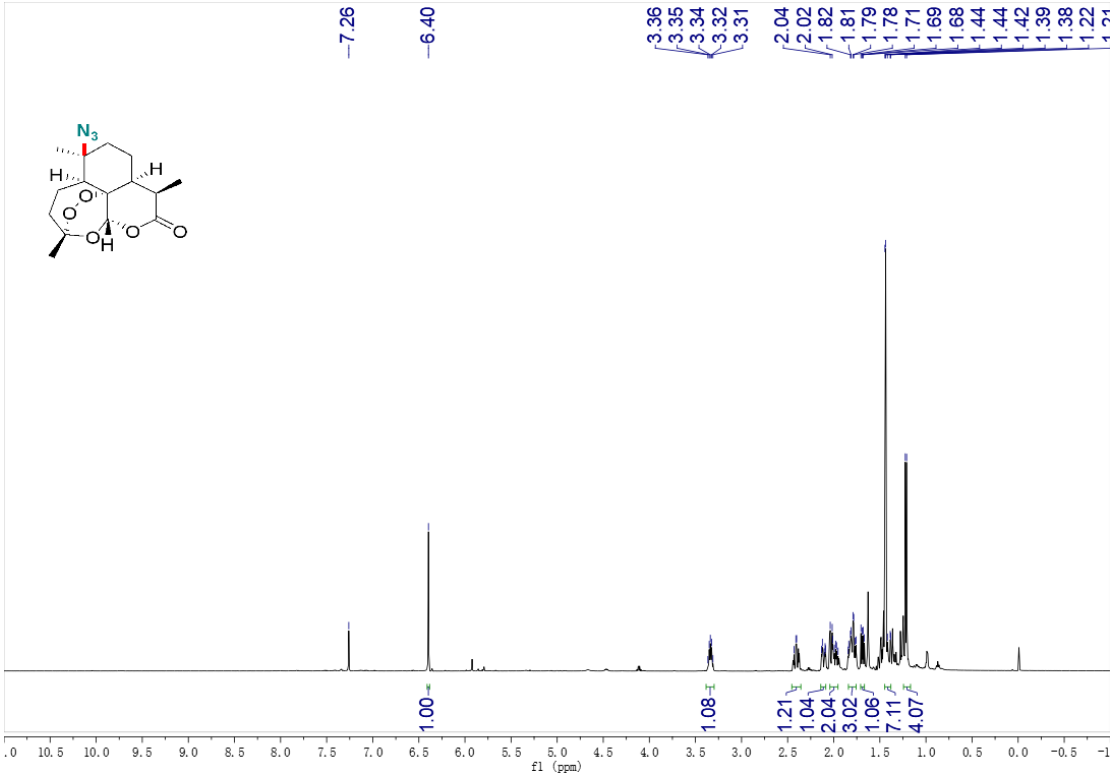
^{13}C NMR of compound **34b** (126 MHz, $CDCl_3$)



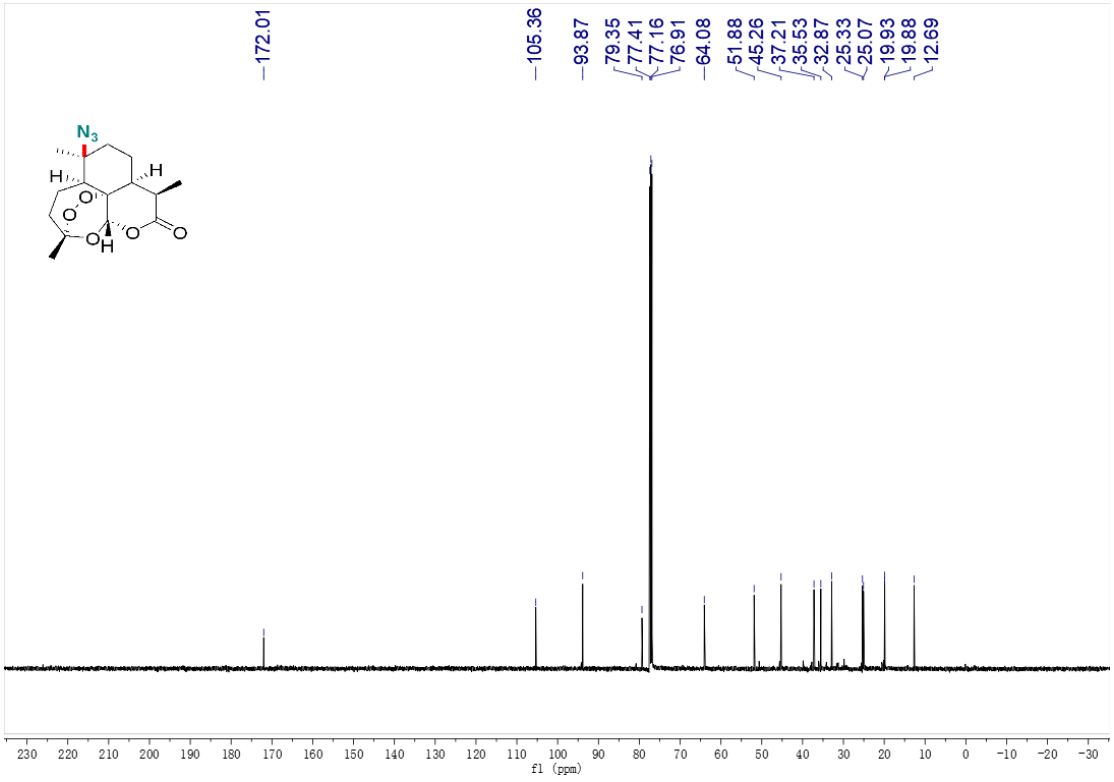
^{1}H NMR of compound **35b** (500 MHz, $CDCl_3$)



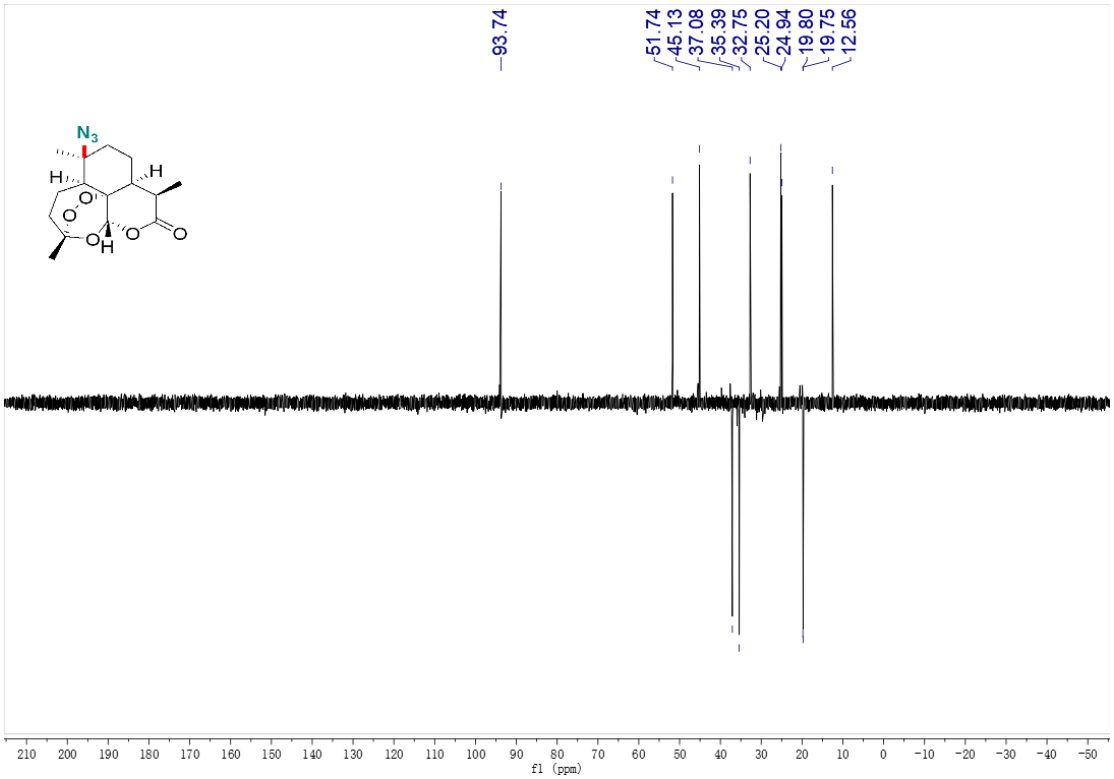
^{13}C NMR of compound **35b** (126 MHz, $CDCl_3$)



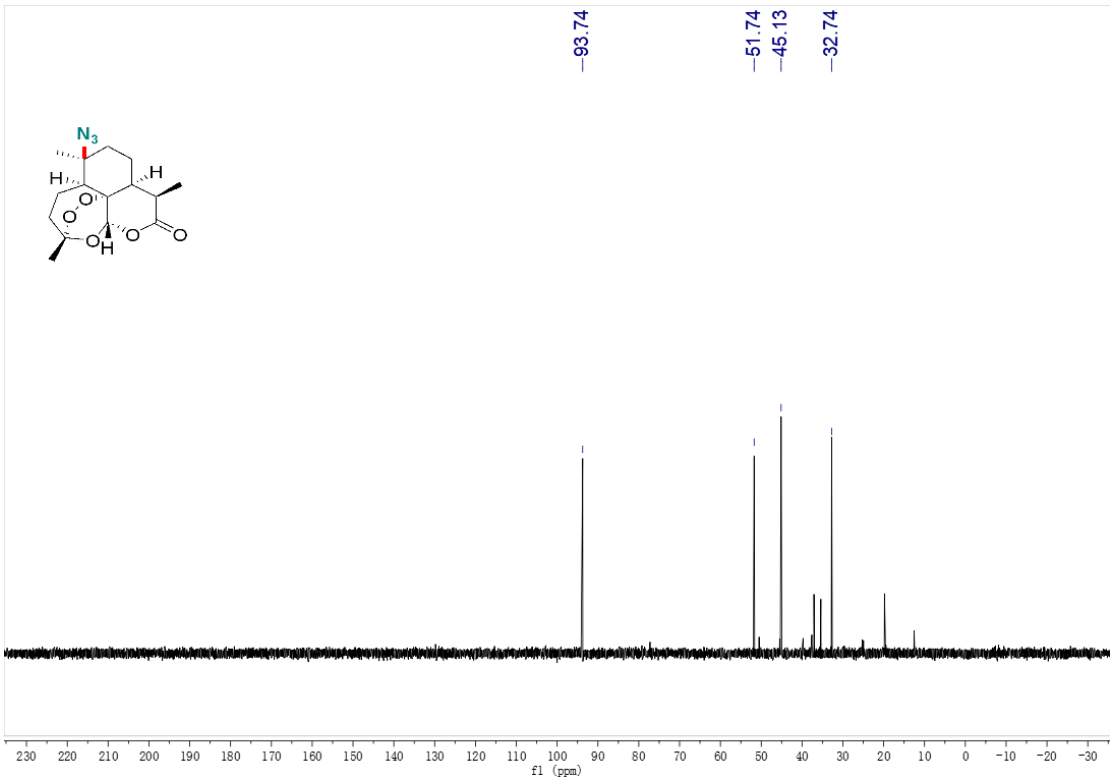
^{1}H NMR of compound **36b** (500 MHz, $CDCl_3$)



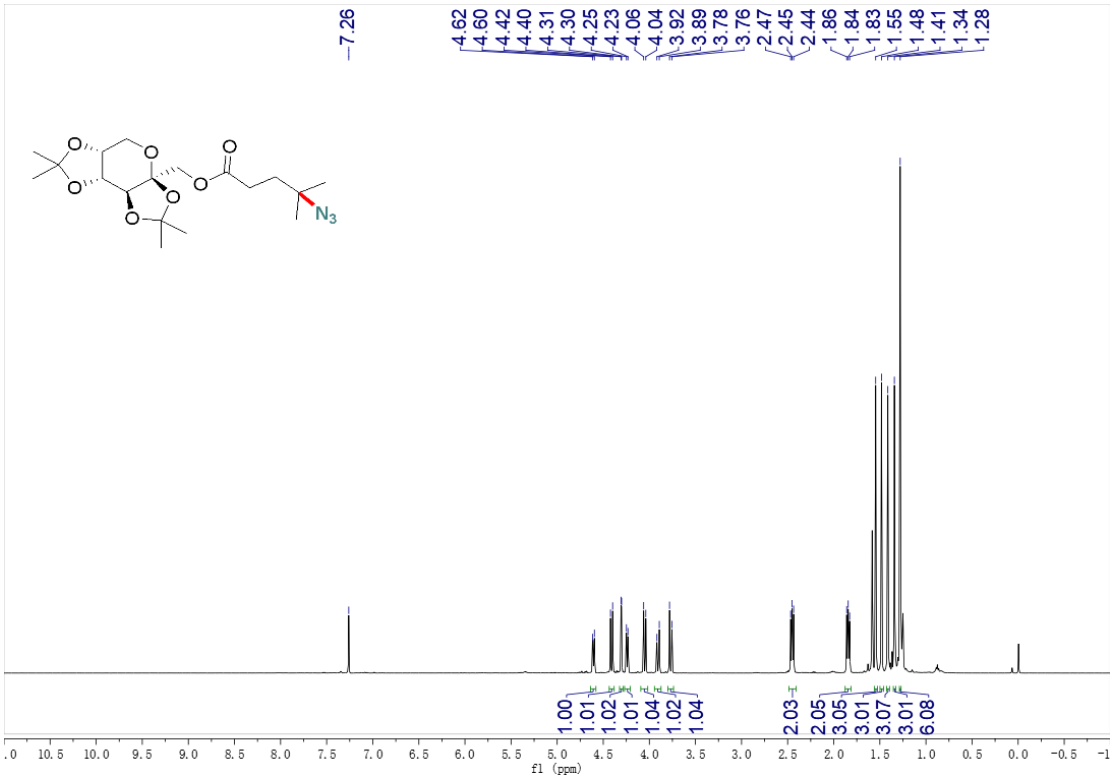
^{13}C NMR of compound **36b** (126 MHz, $CDCl_3$)



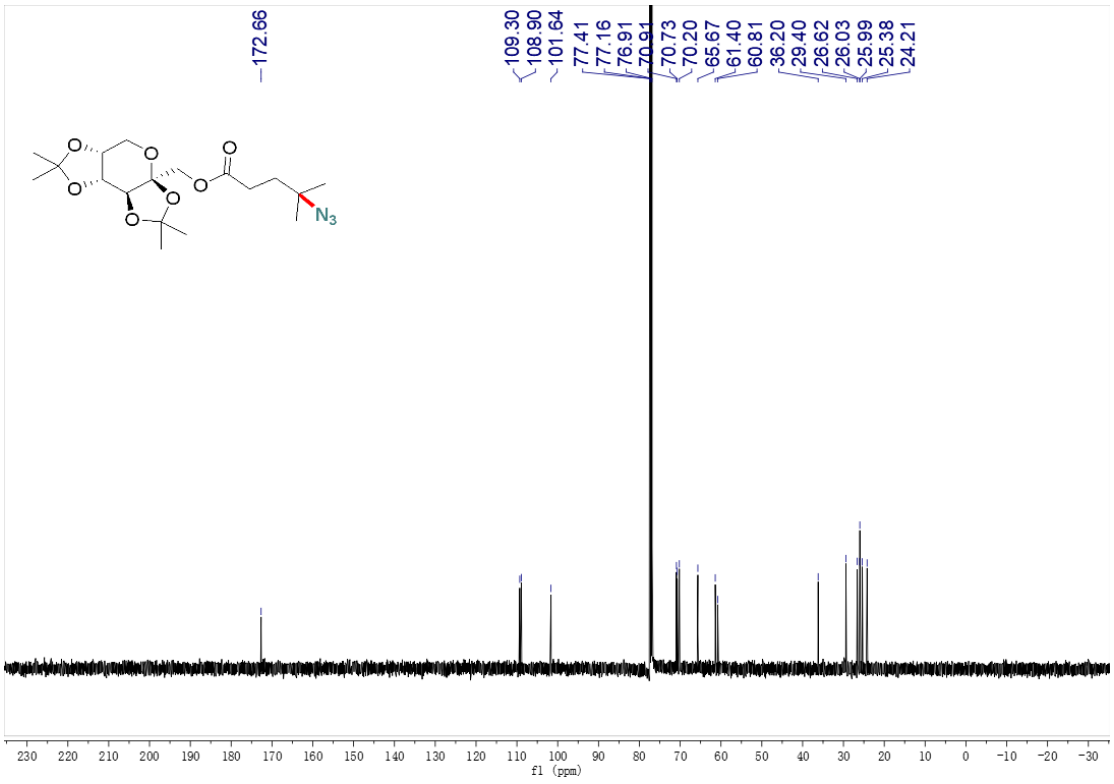
DEPT 135 of compound **36b** (126 MHz, $CDCl_3$)



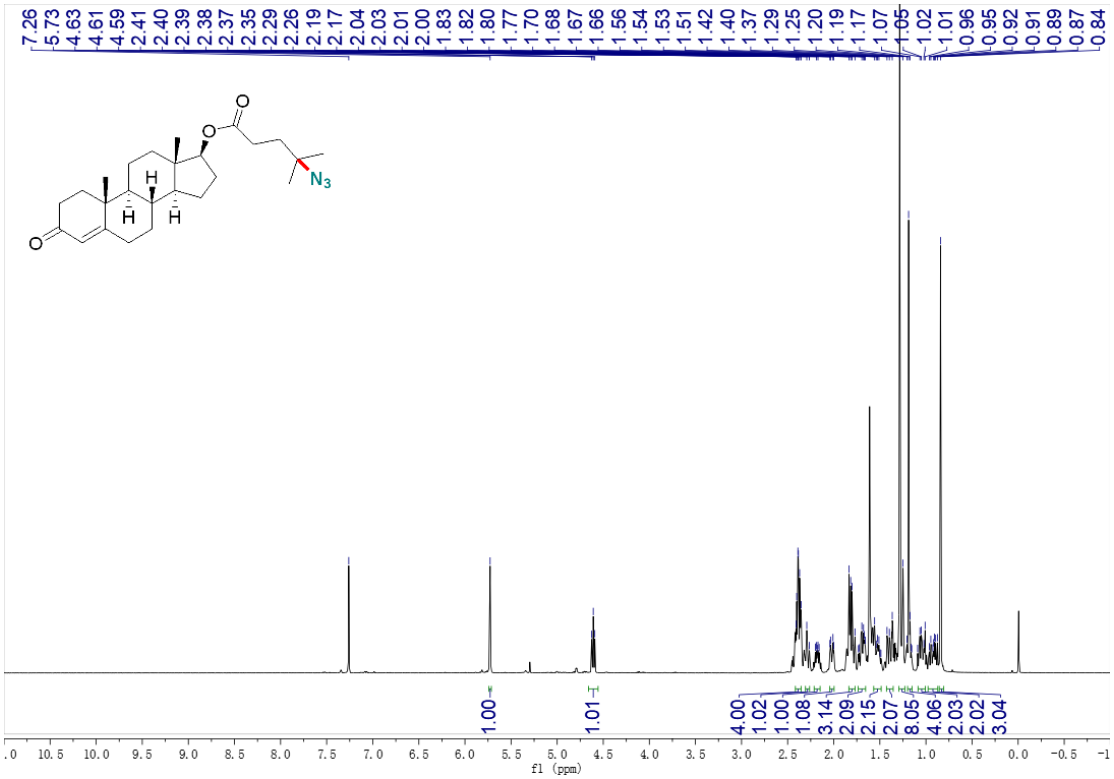
DEPT 90 of compound **36b** (126 MHz, $CDCl_3$)



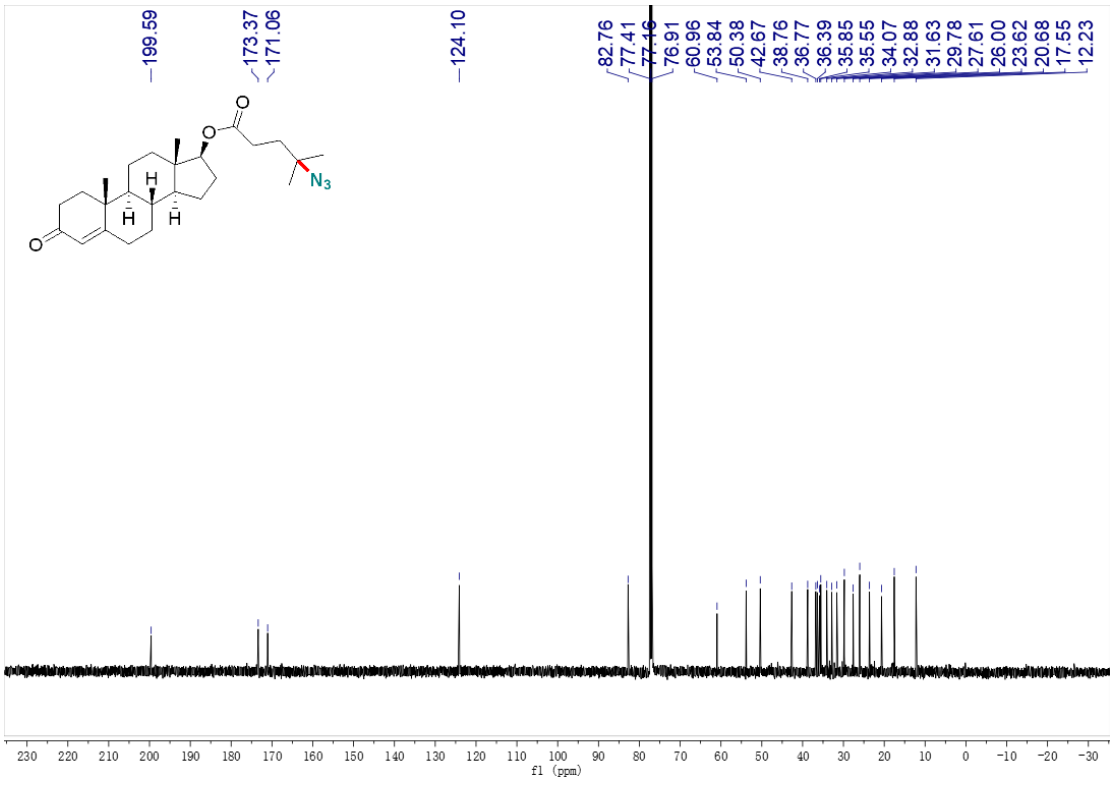
^{1}H NMR of compound **37b** (500 MHz, $CDCl_3$)



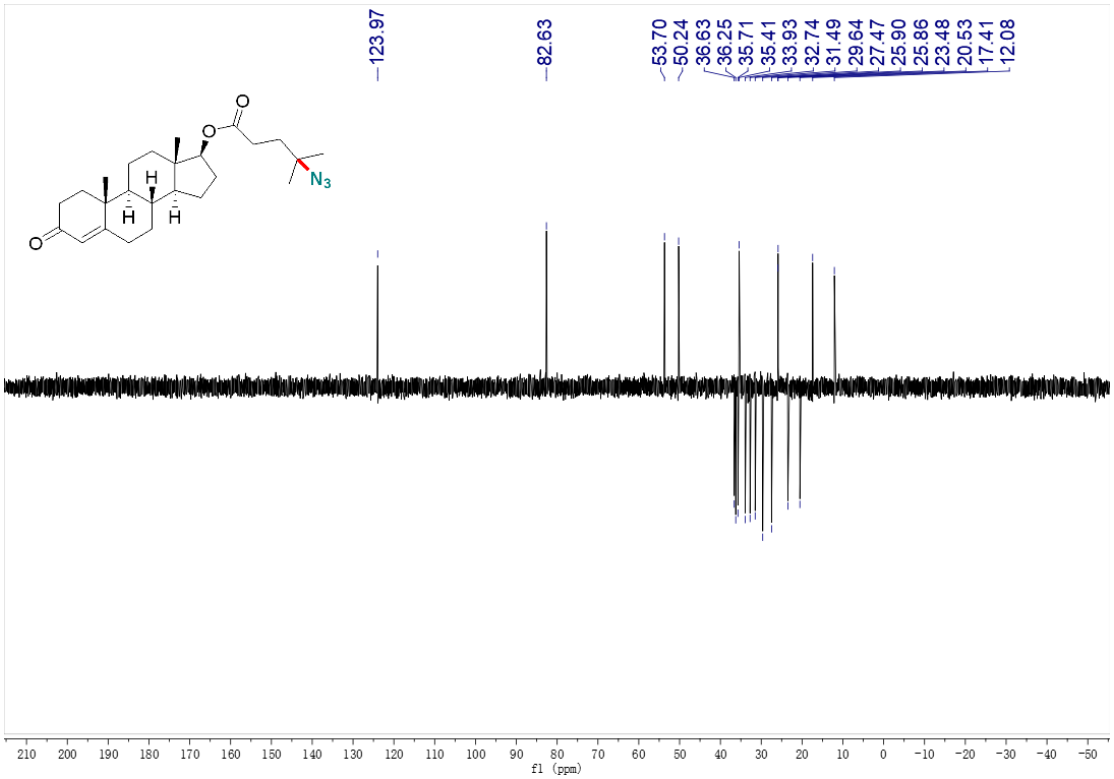
^{13}C NMR of compound **37b** (126 MHz, $CDCl_3$)



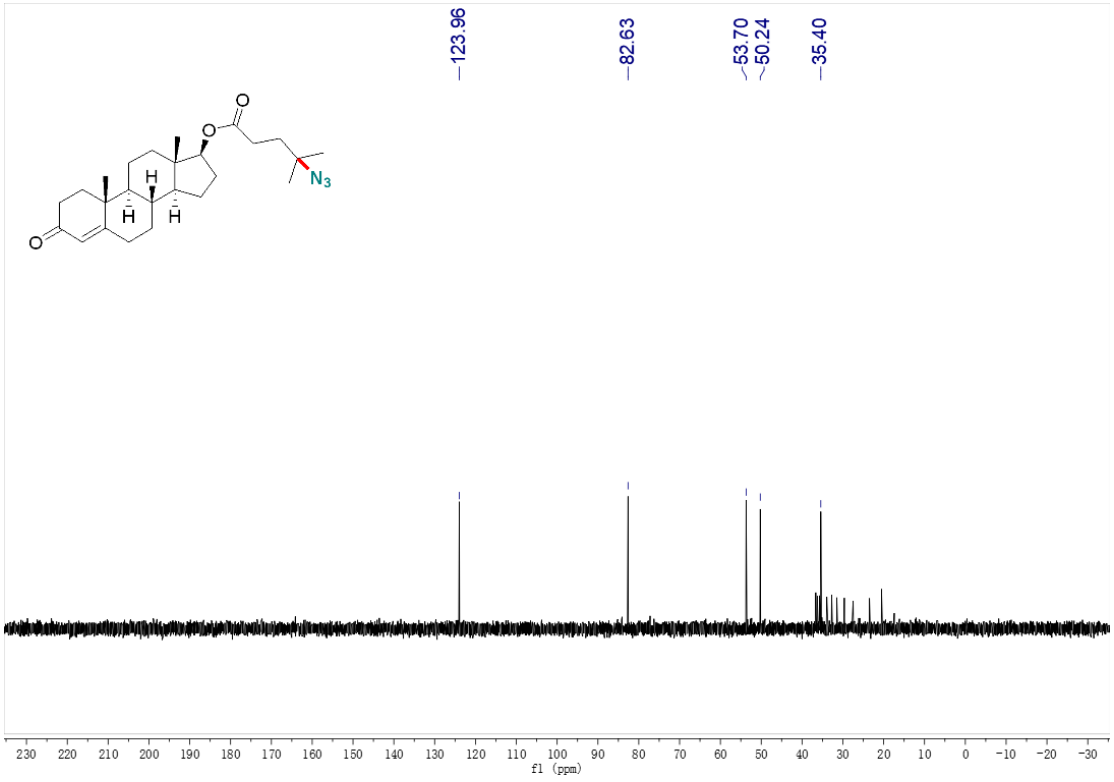
^{1}H NMR of compound **38b** (500 MHz, $CDCl_3$)



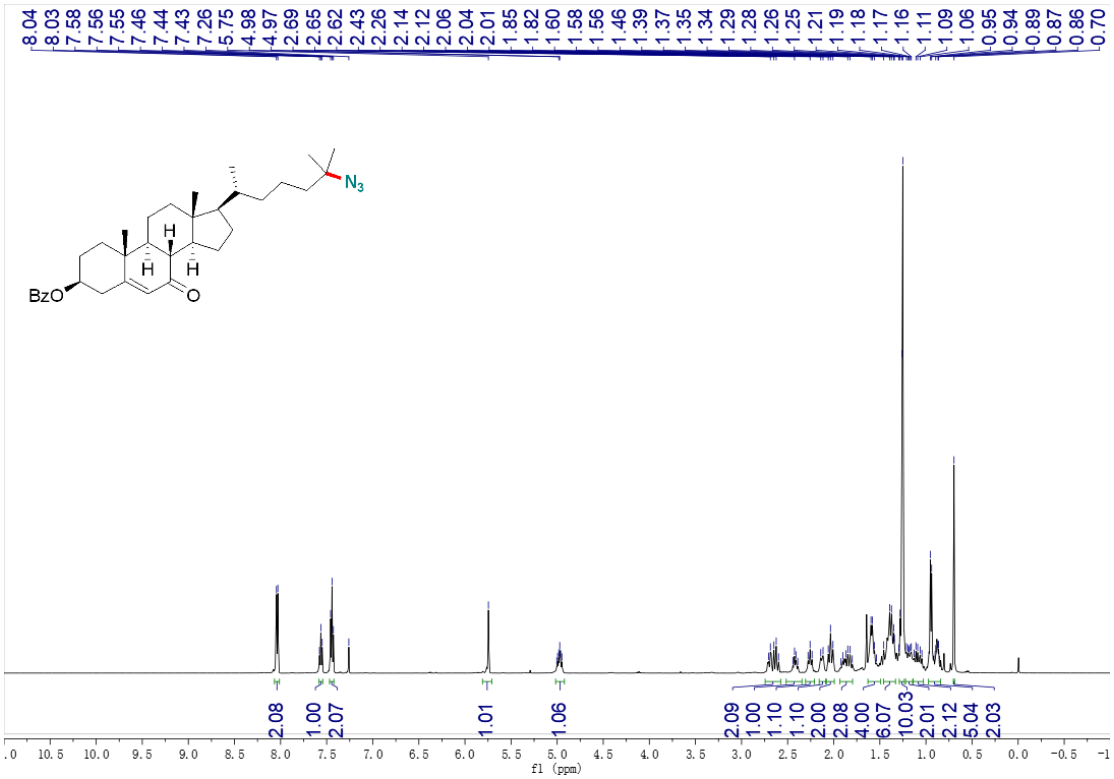
^{13}C NMR of compound **38b** (126 MHz, $CDCl_3$)



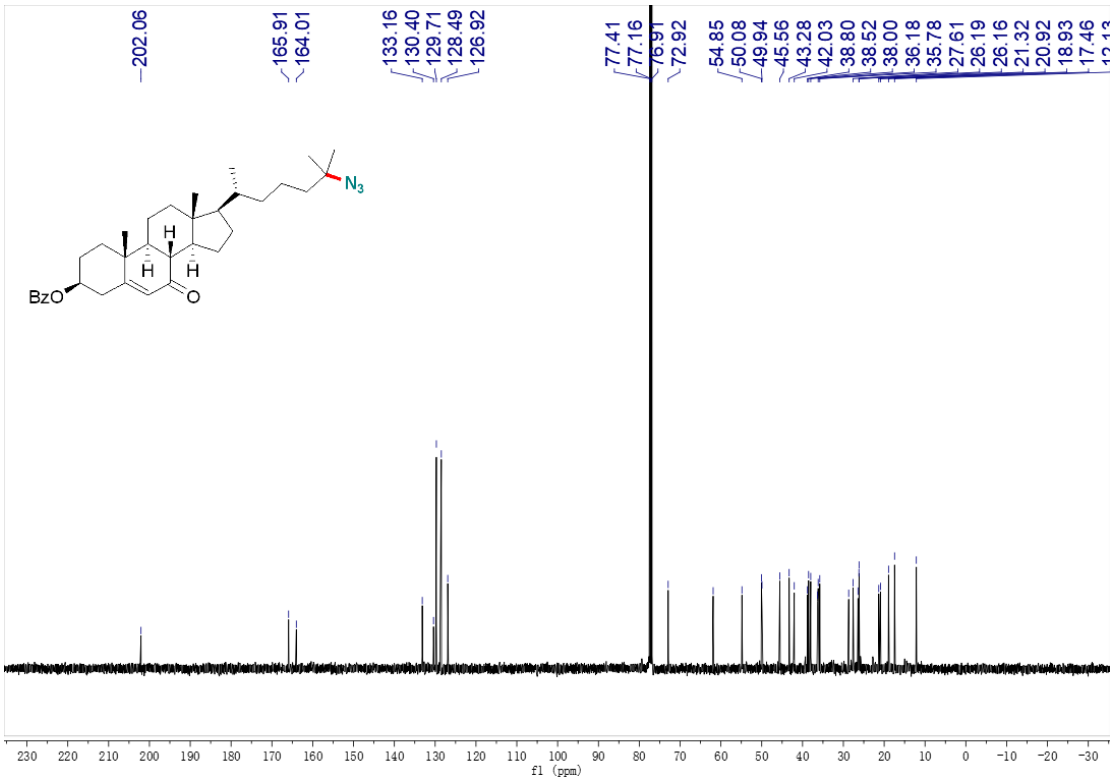
DEPT 135 of compound **38b** (126 MHz, $CDCl_3$)



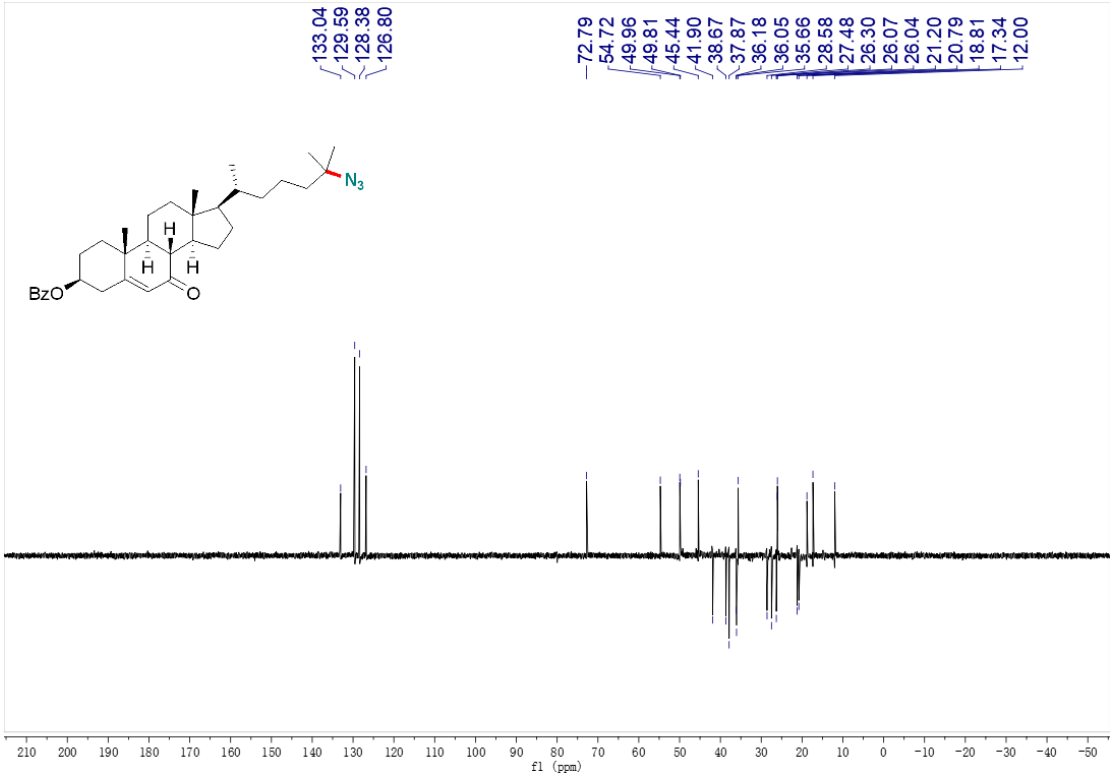
DEPT 90 of compound **38b** (126 MHz, $CDCl_3$)



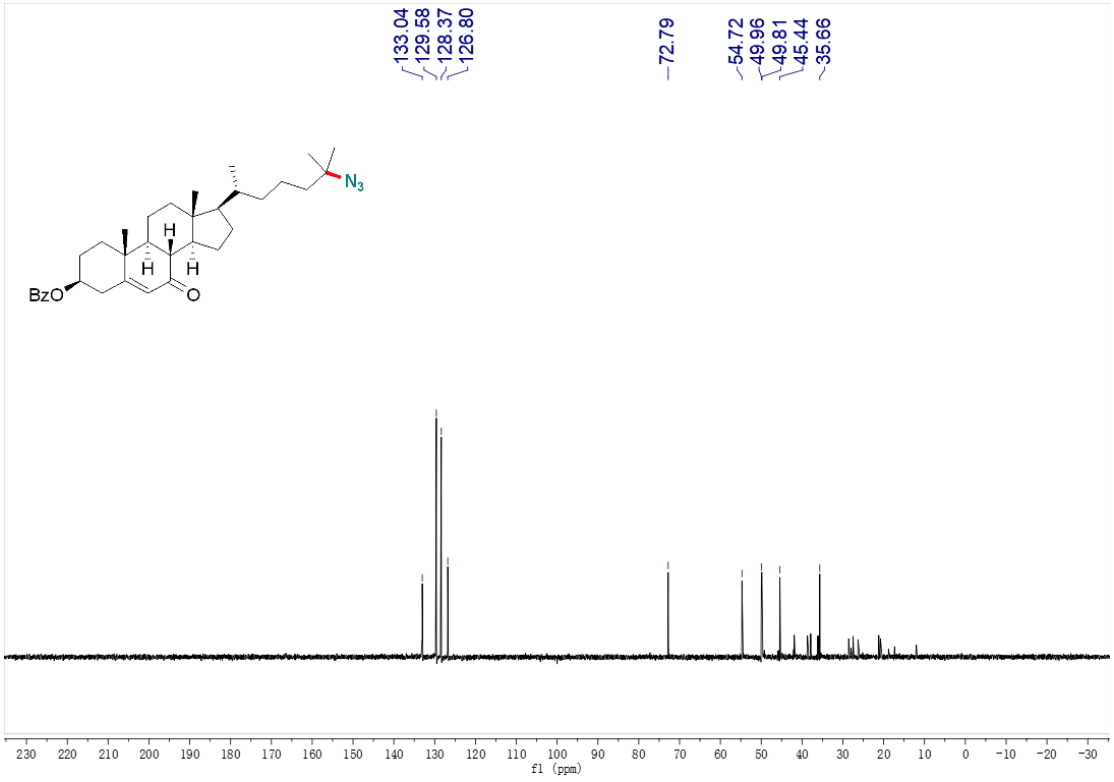
^{1}H NMR of compound **39b** (500 MHz, $CDCl_3$)



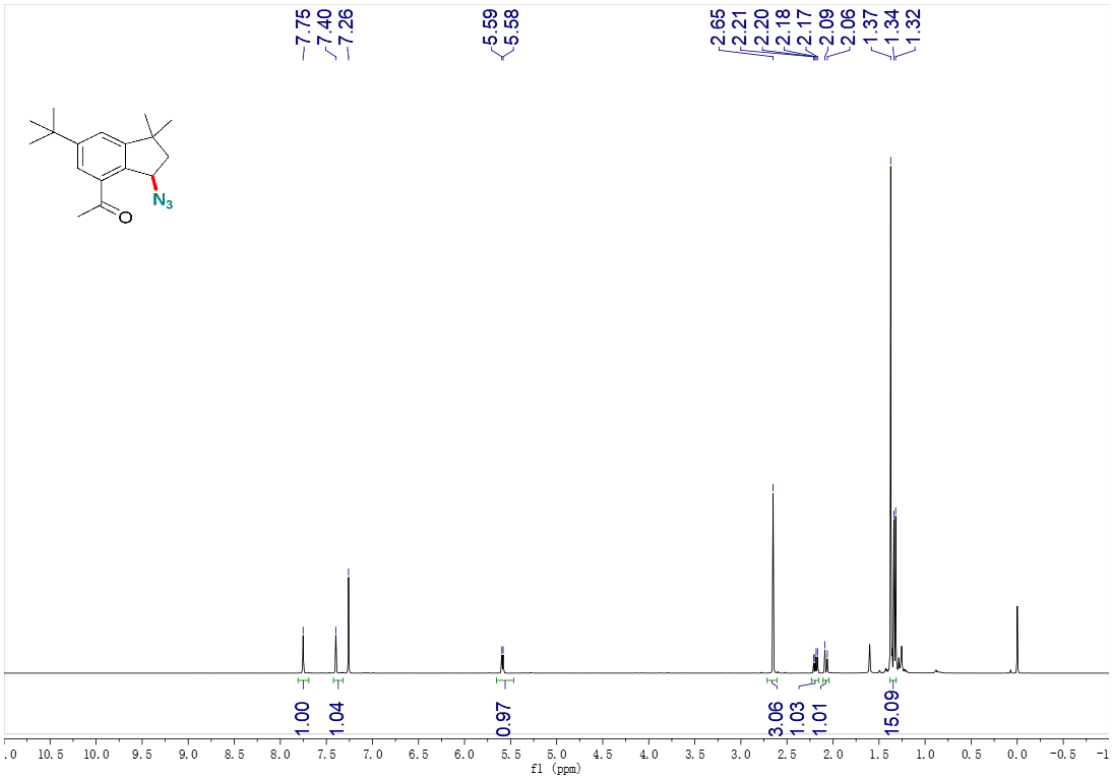
^{13}C NMR of compound **39b** (126 MHz, $CDCl_3$)



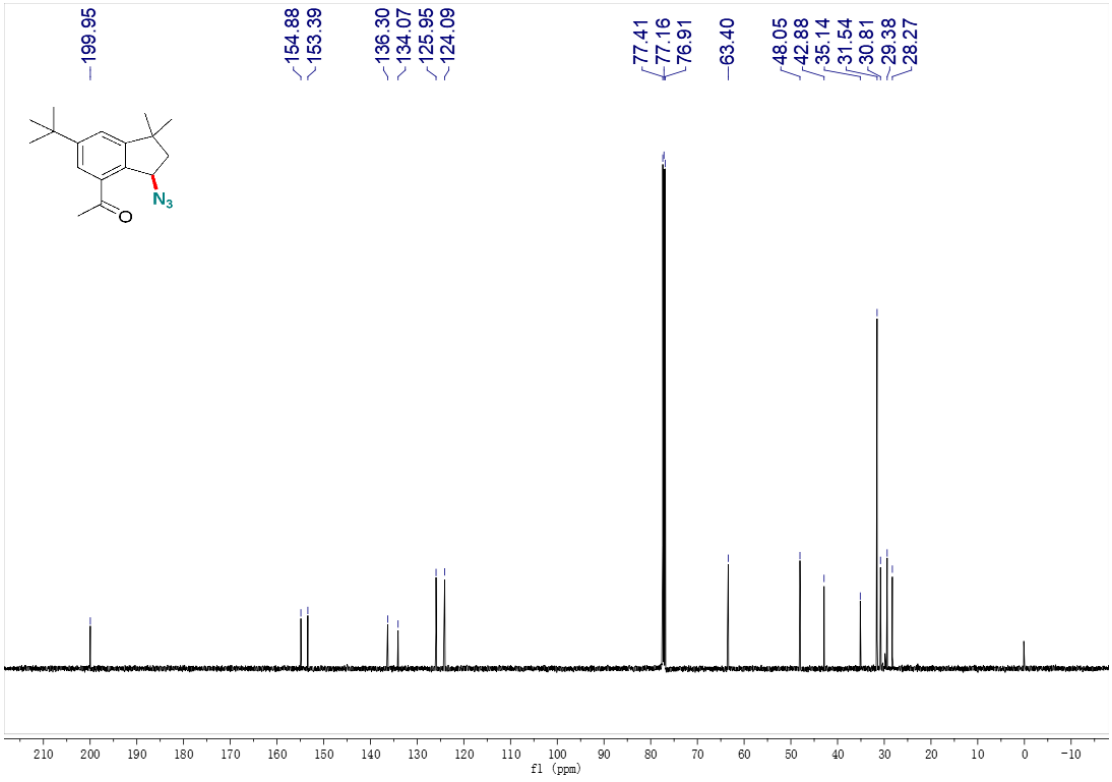
DEPT 135 of compound **39b** (126 MHz, $CDCl_3$)



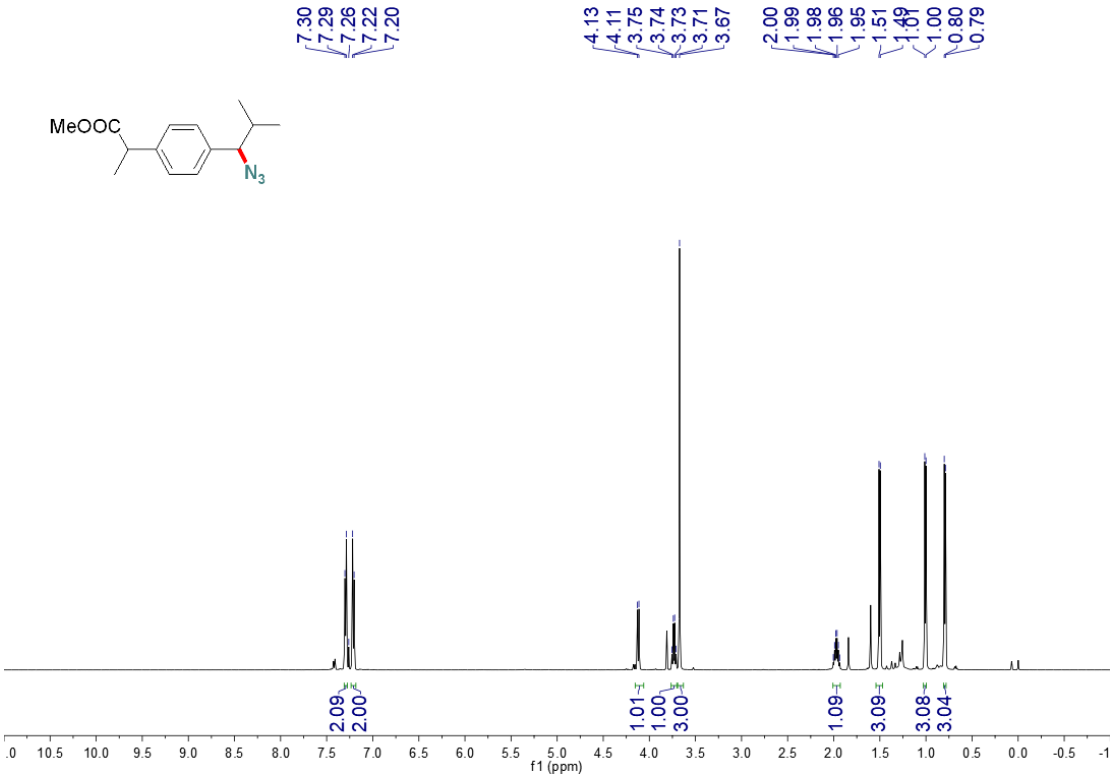
DEPT 90 of compound **39b** (126 MHz, $CDCl_3$)



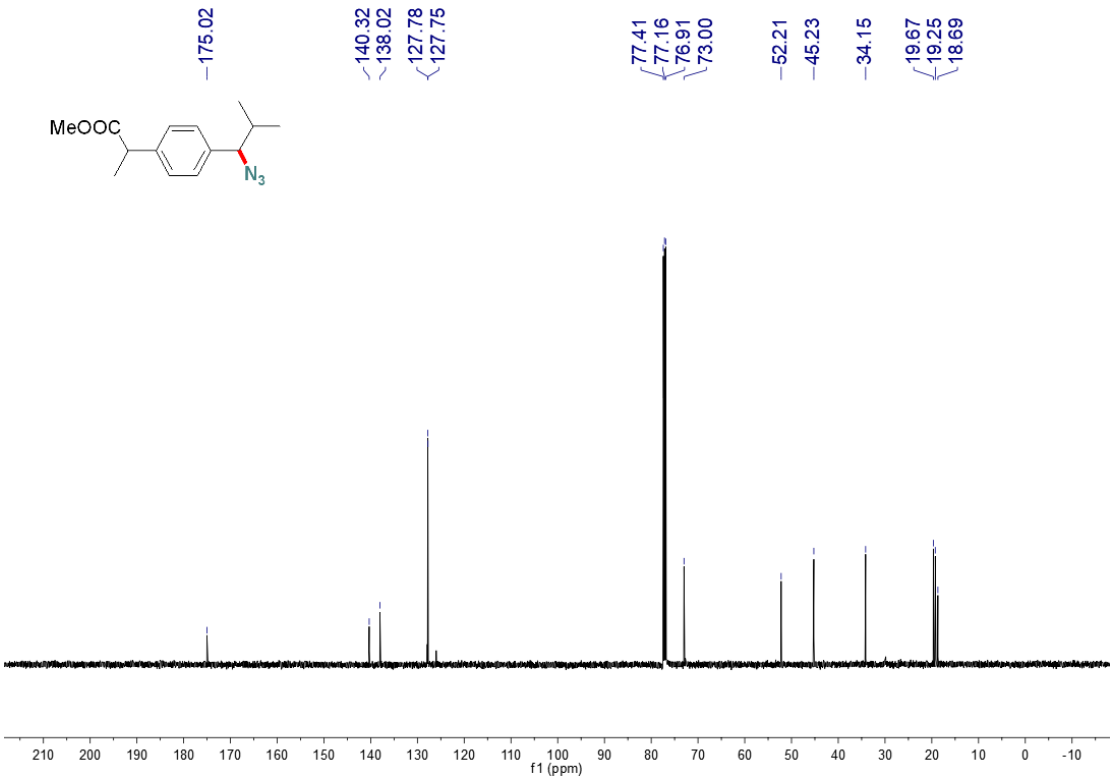
^{1}H NMR of compound **40b** (500 MHz, $CDCl_3$)



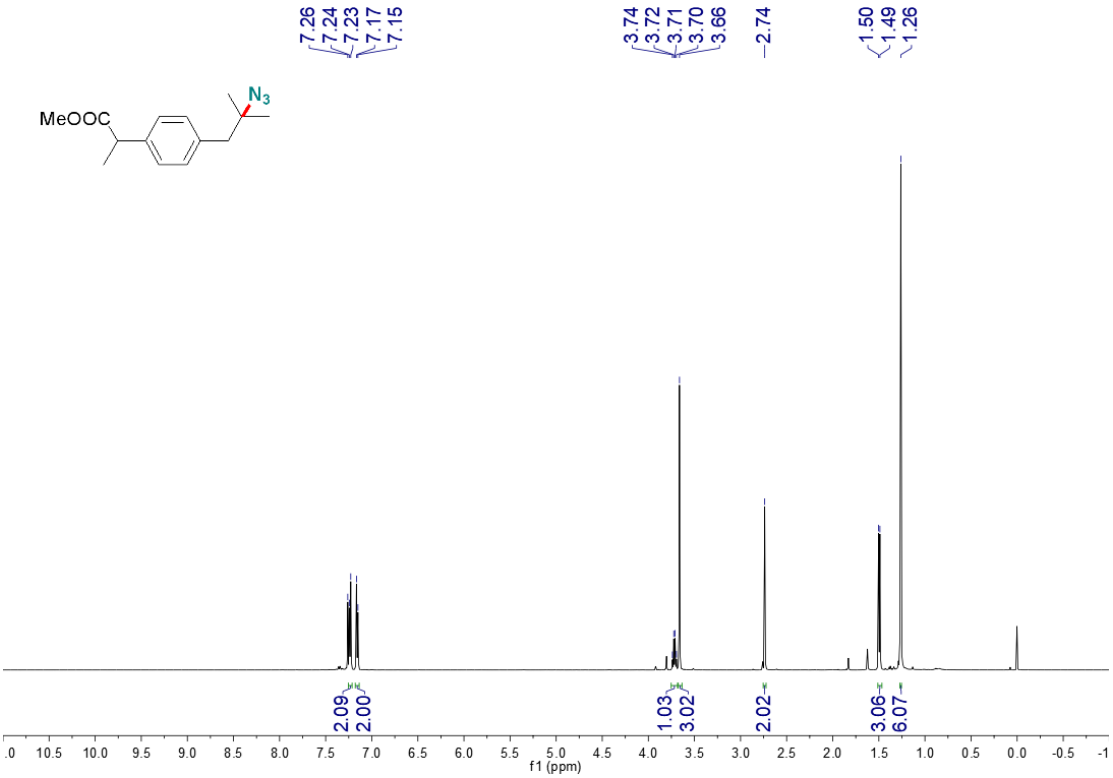
^{13}C NMR of compound **40b** (126 MHz, $CDCl_3$)



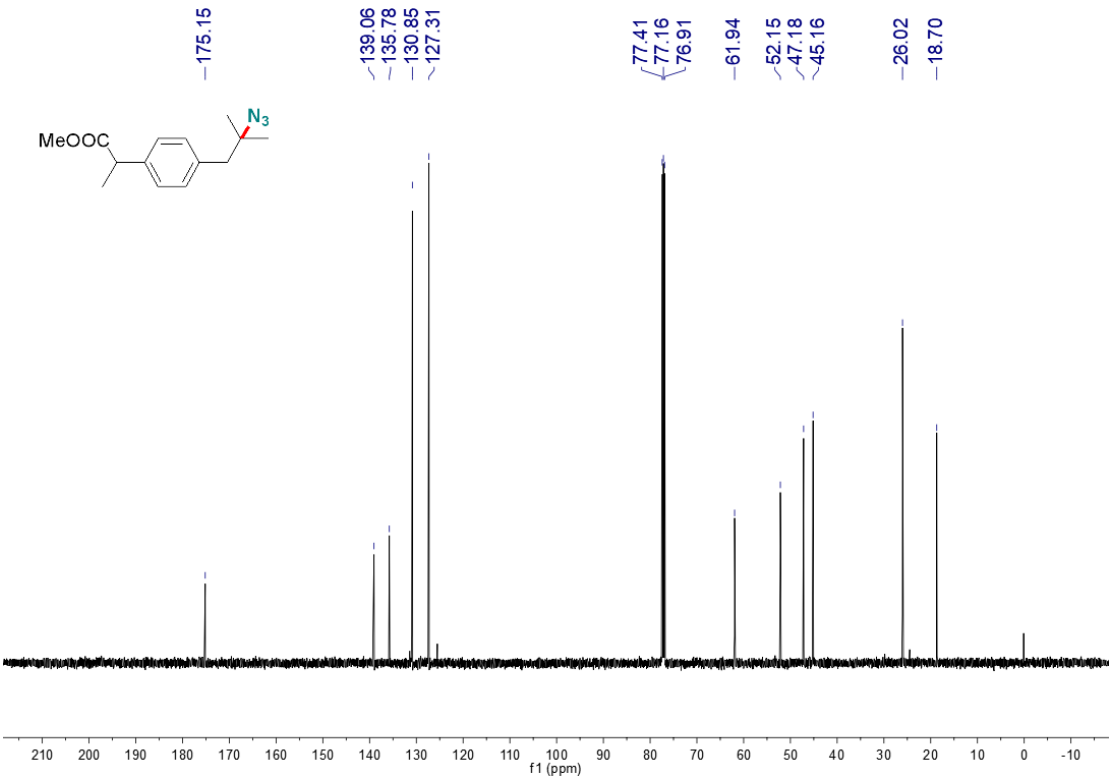
^{1}H NMR of compound **41b** (500 MHz, $CDCl_3$)



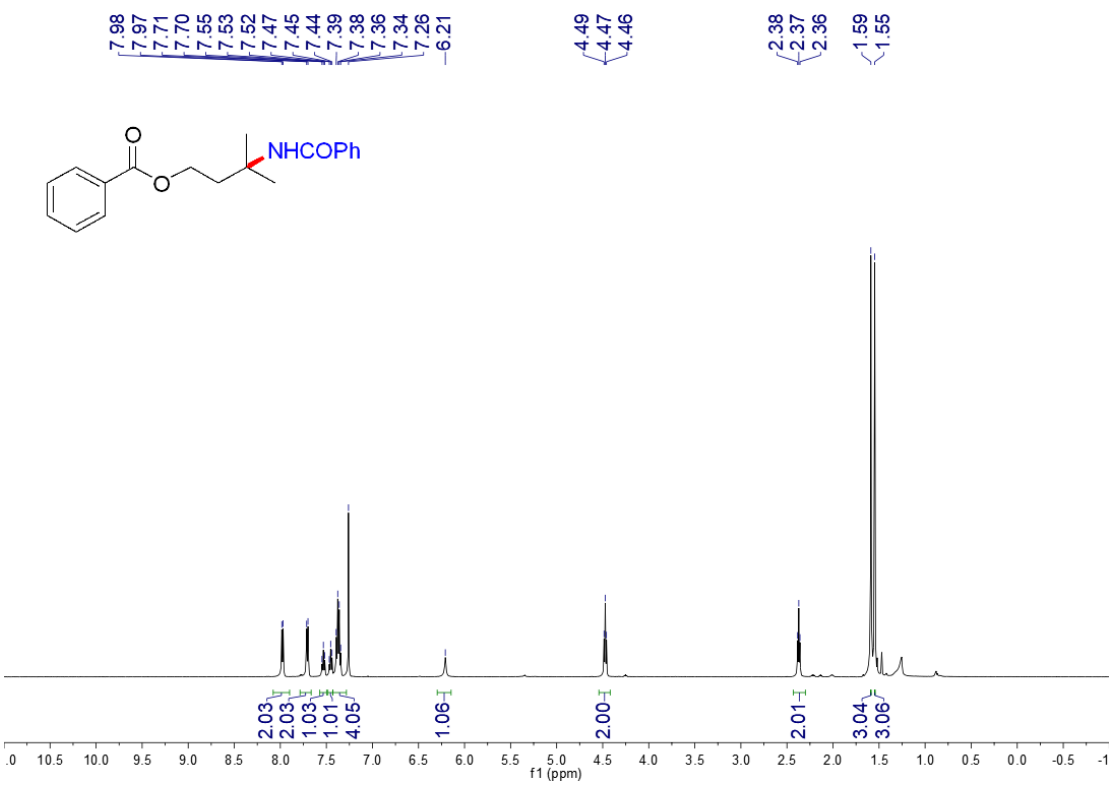
^{13}C NMR of compound **41b** (126 MHz, $CDCl_3$)



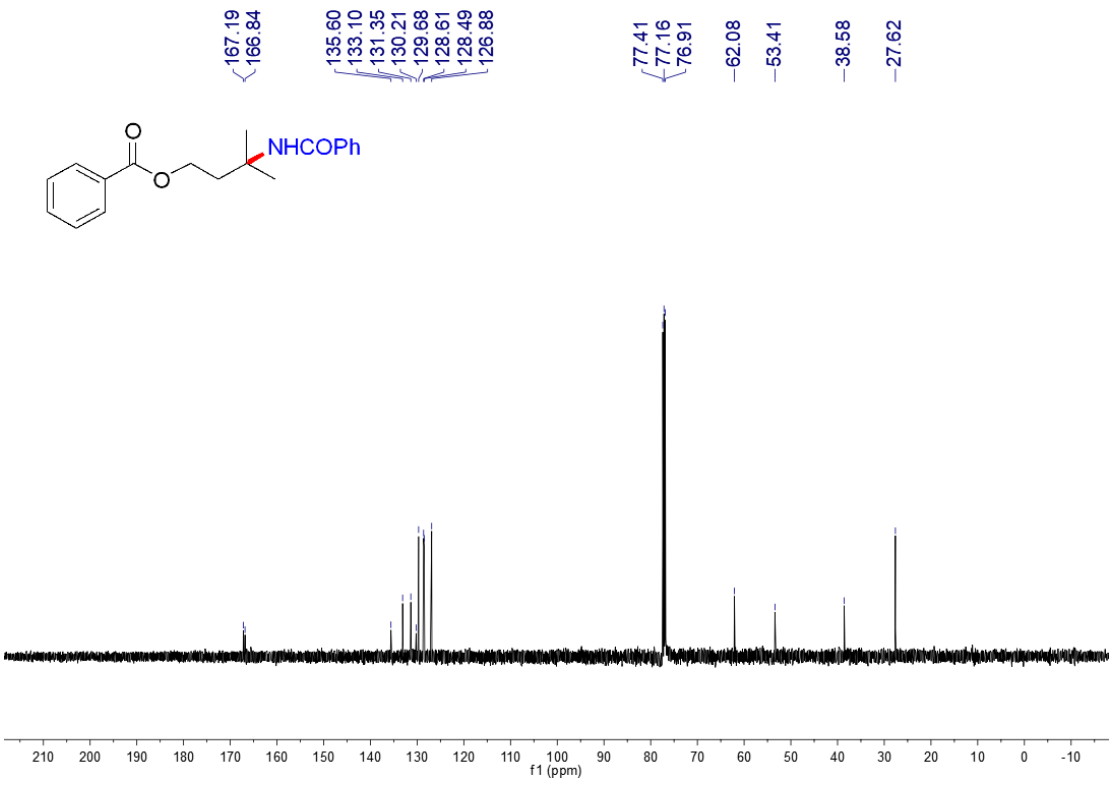
^{1}H NMR of compound **41b'** (500 MHz, $CDCl_3$)



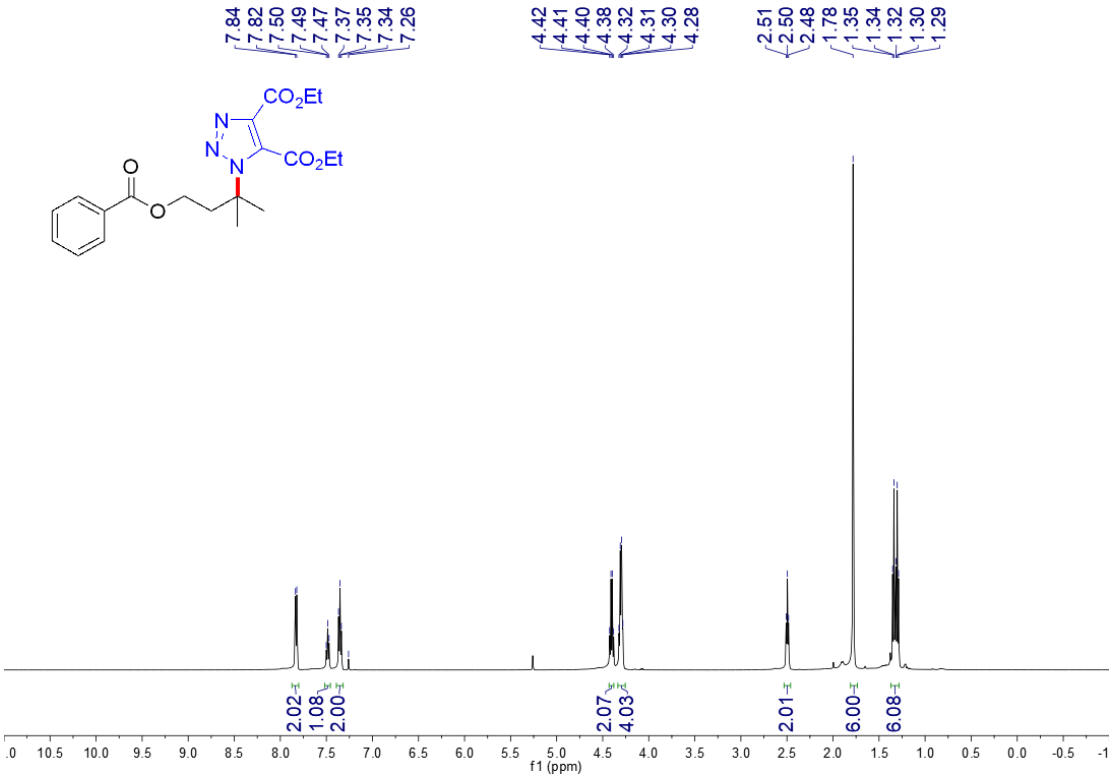
^{13}C NMR of compound **41b'** (126 MHz, $CDCl_3$)



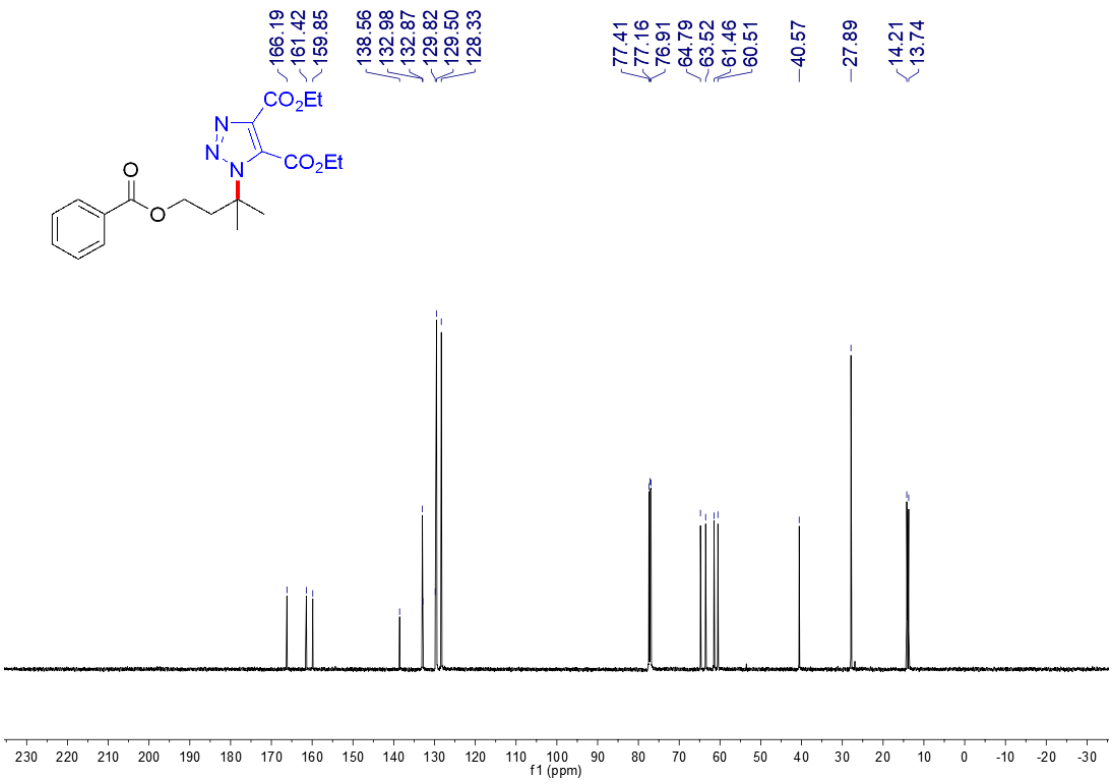
^{1}H NMR of compound **42** (500 MHz, $CDCl_3$)



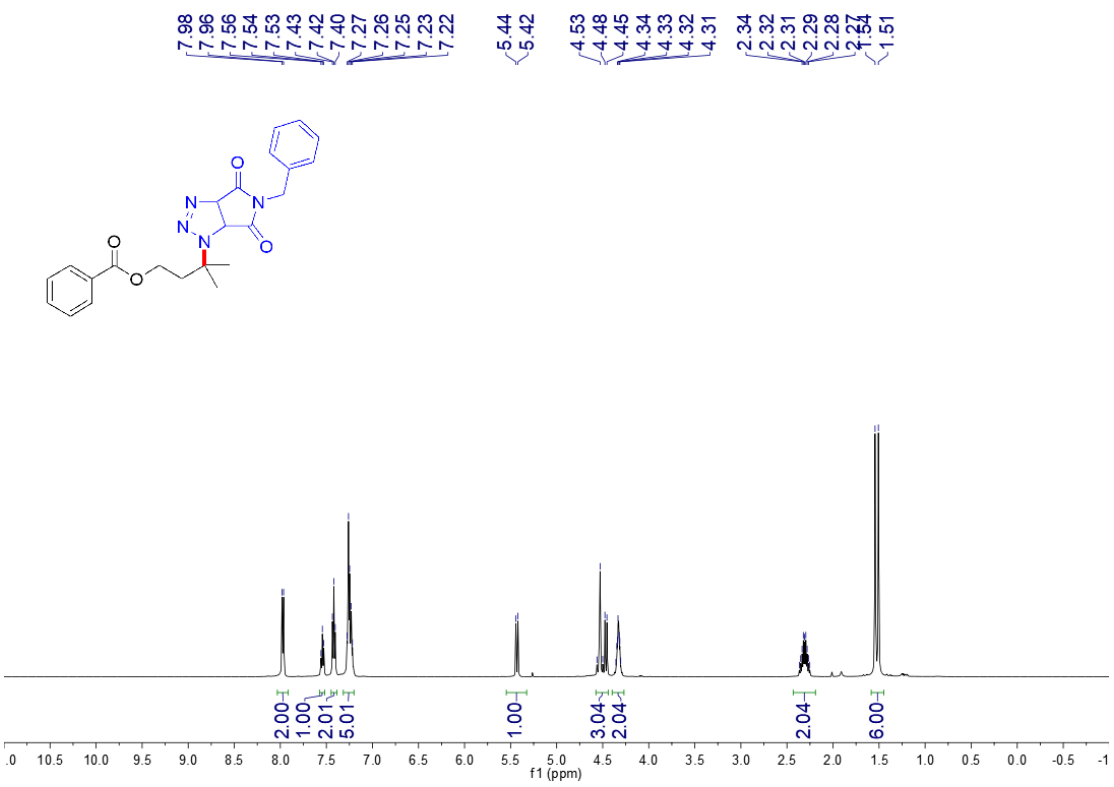
^{13}C NMR of compound **42** (126 MHz, $CDCl_3$)



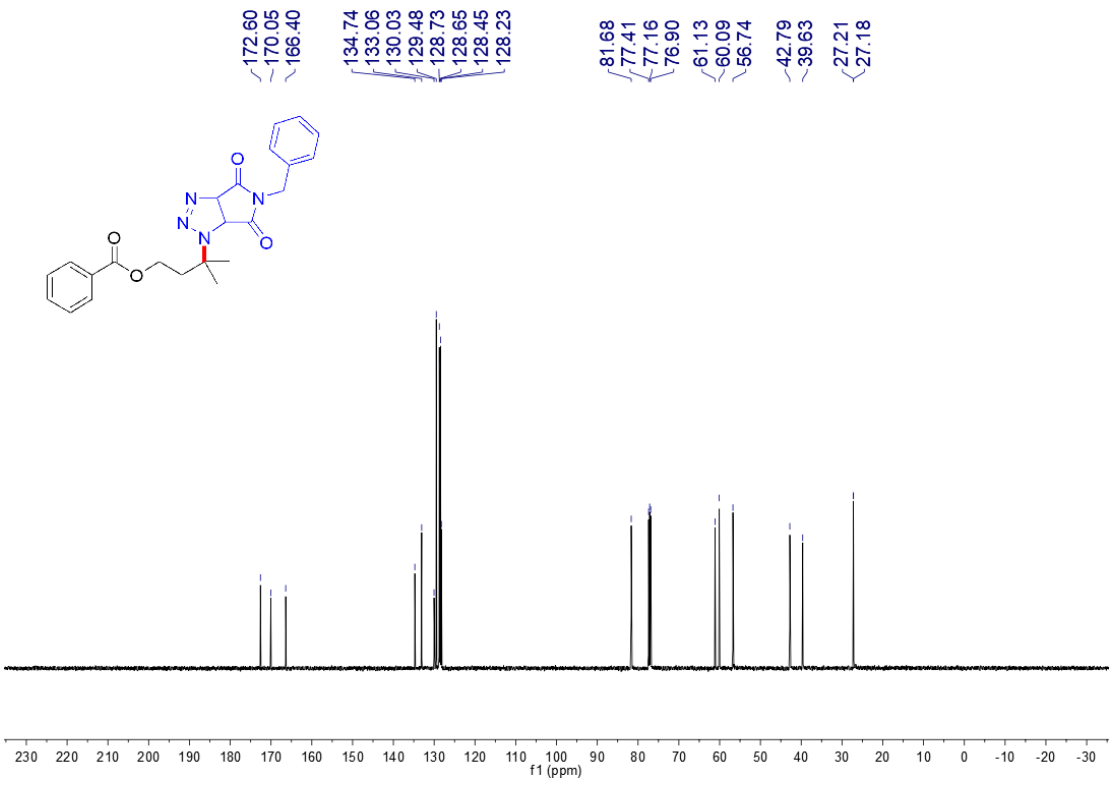
^{1}H NMR of compound **43** (500 MHz, $CDCl_3$)



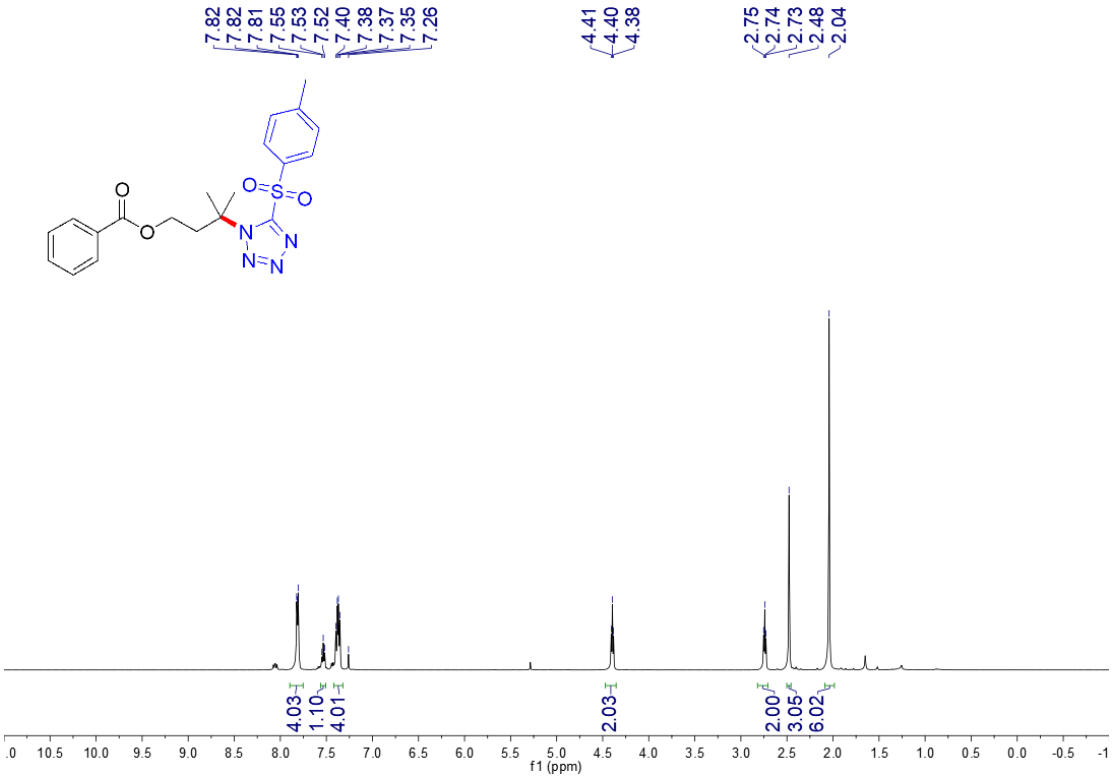
^{13}C NMR of compound **43** (126 MHz, $CDCl_3$)



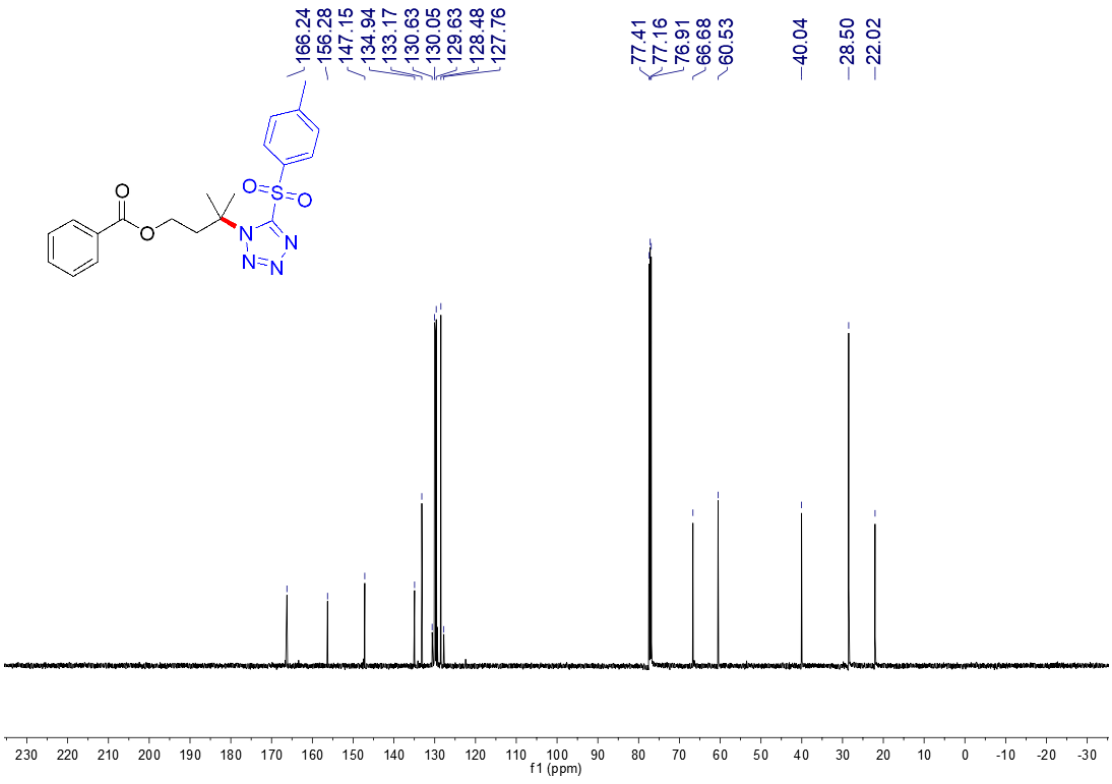
^{1}H NMR of compound **44** (500 MHz, $CDCl_3$)



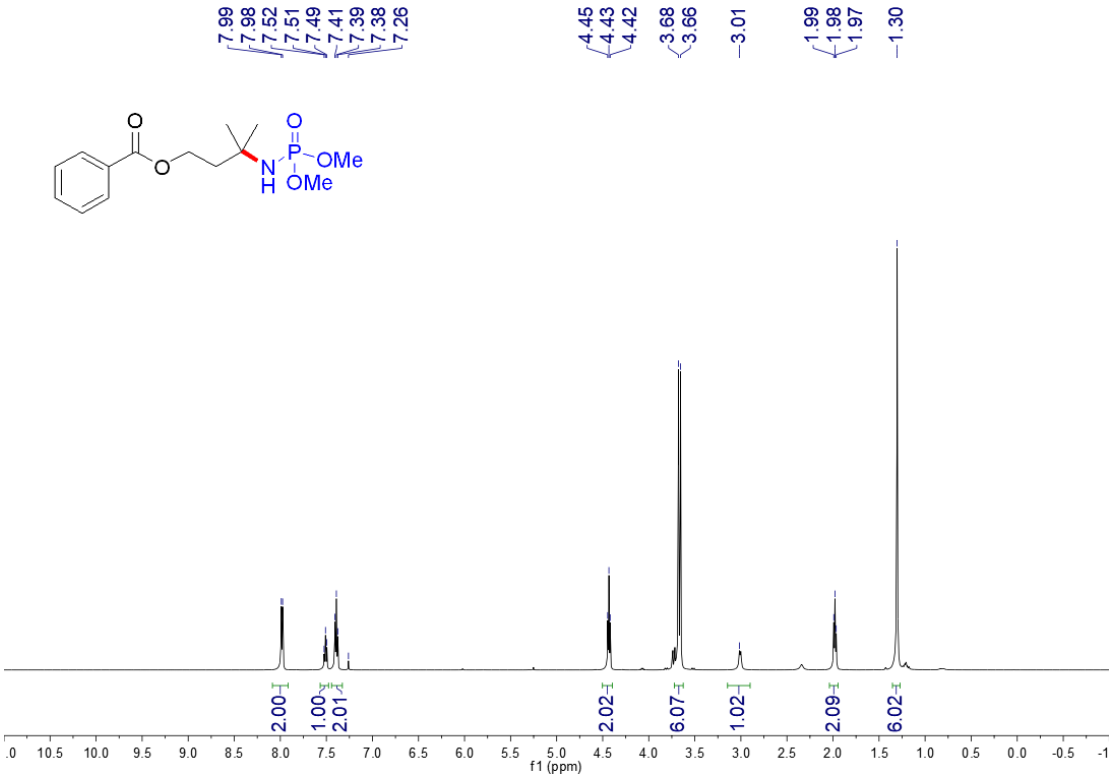
^{13}C NMR of compound **44** (126 MHz, $CDCl_3$)



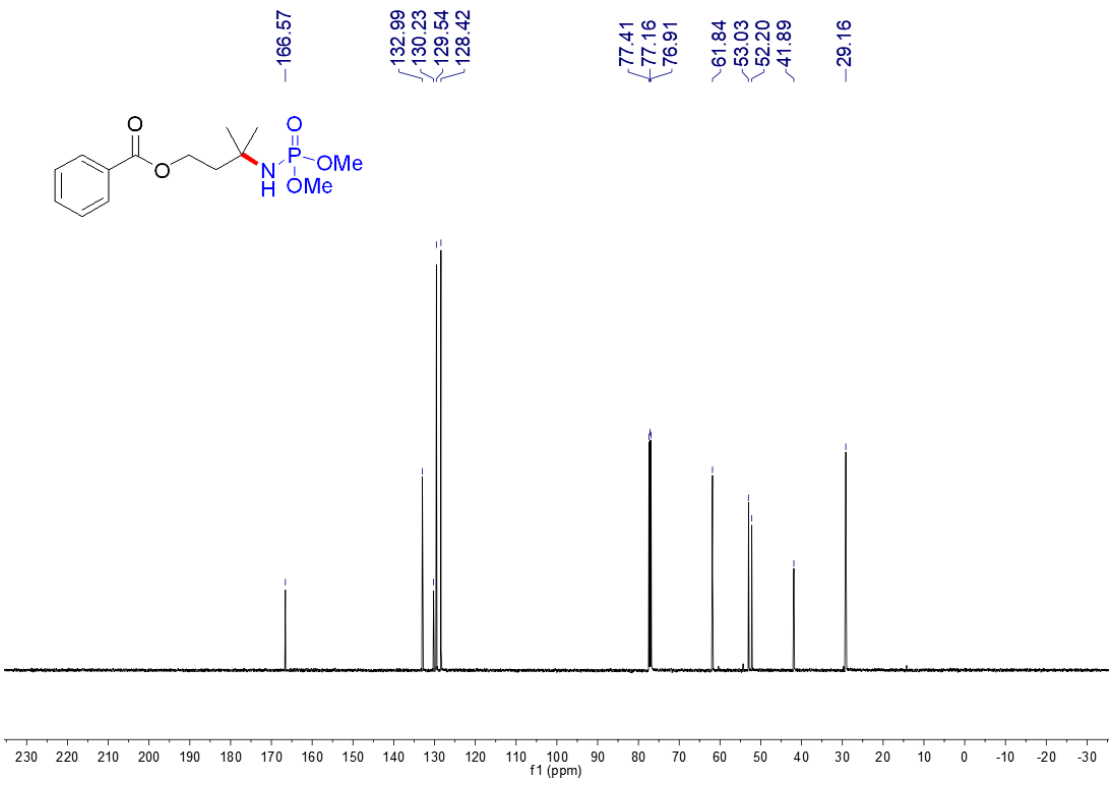
^{1}H NMR of compound **45** (500 MHz, $CDCl_3$)



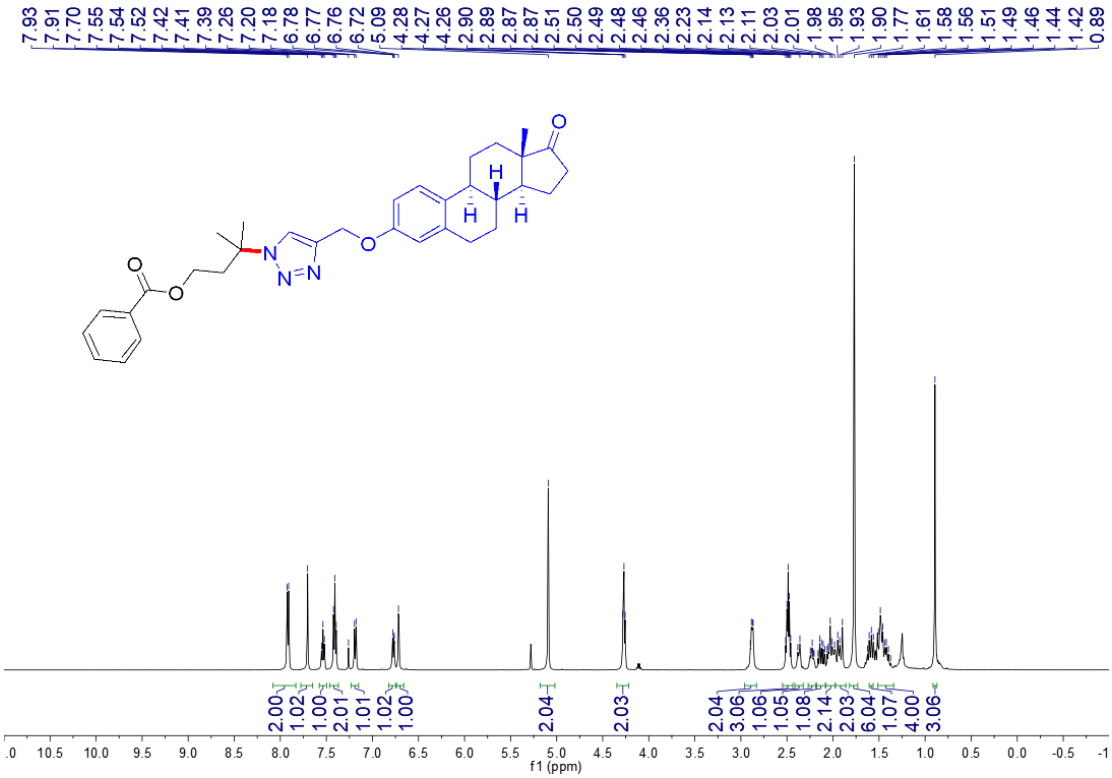
^{13}C NMR of compound **45** (126 MHz, $CDCl_3$)



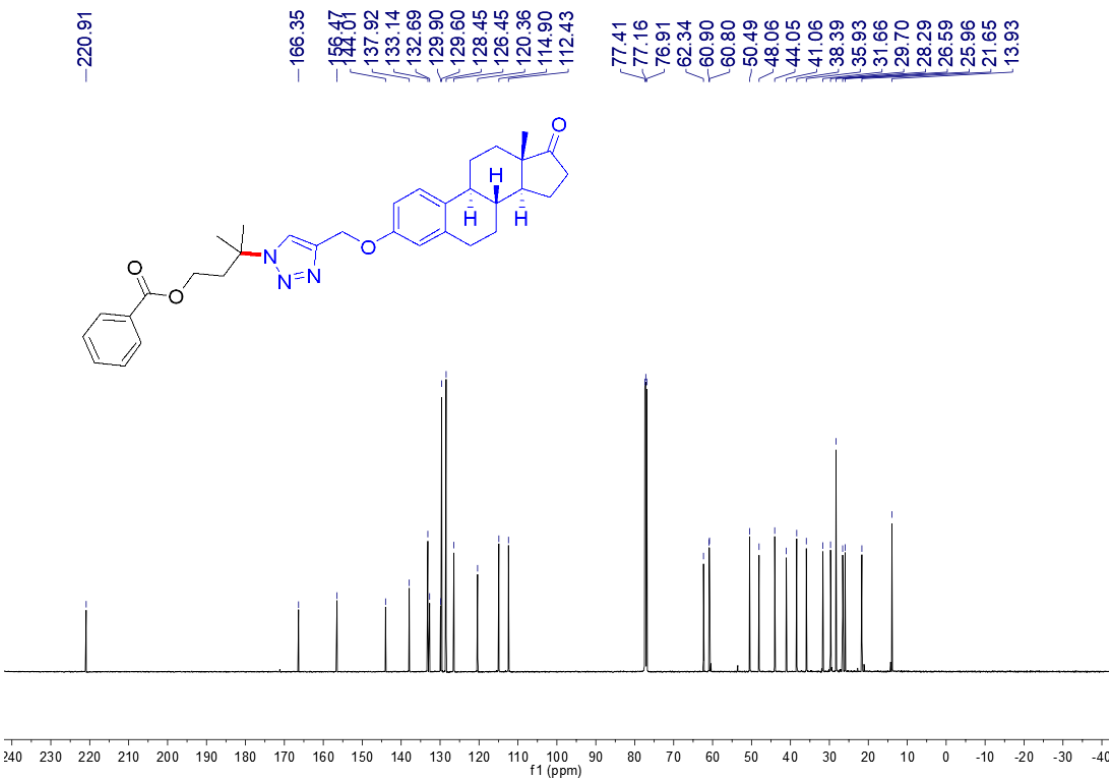
^{1}H NMR of compound **46** (500 MHz, $CDCl_3$)



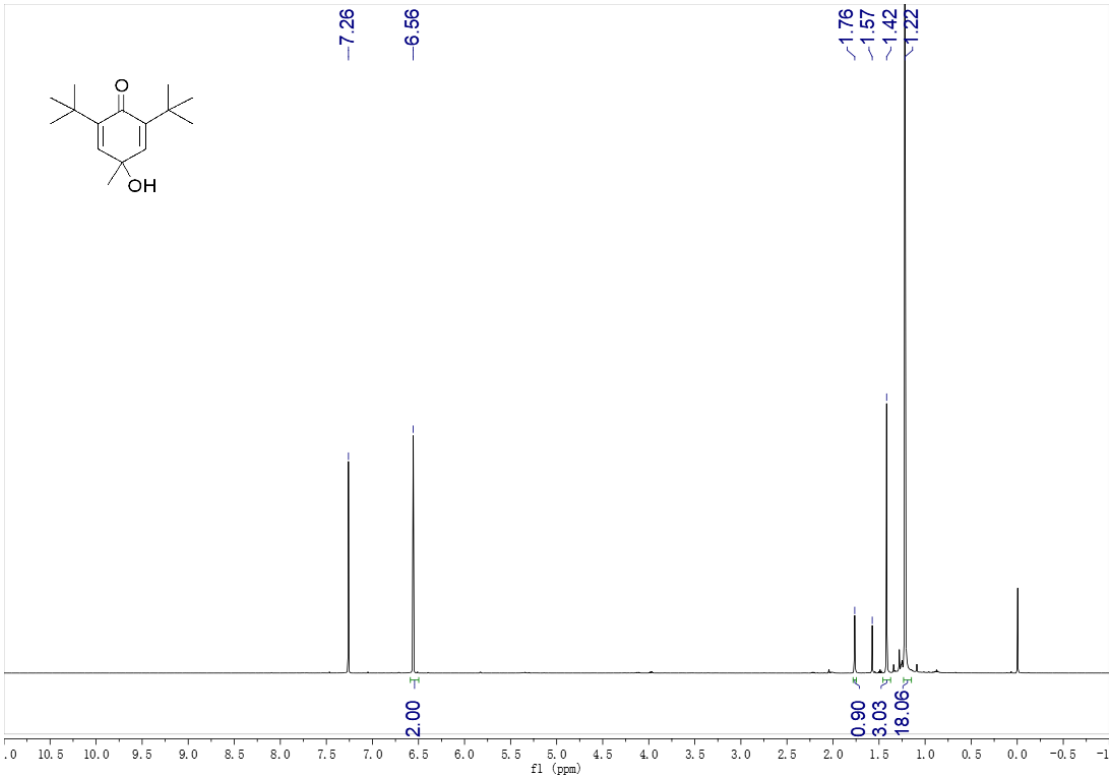
^{13}C NMR of compound **46** (126 MHz, $CDCl_3$)



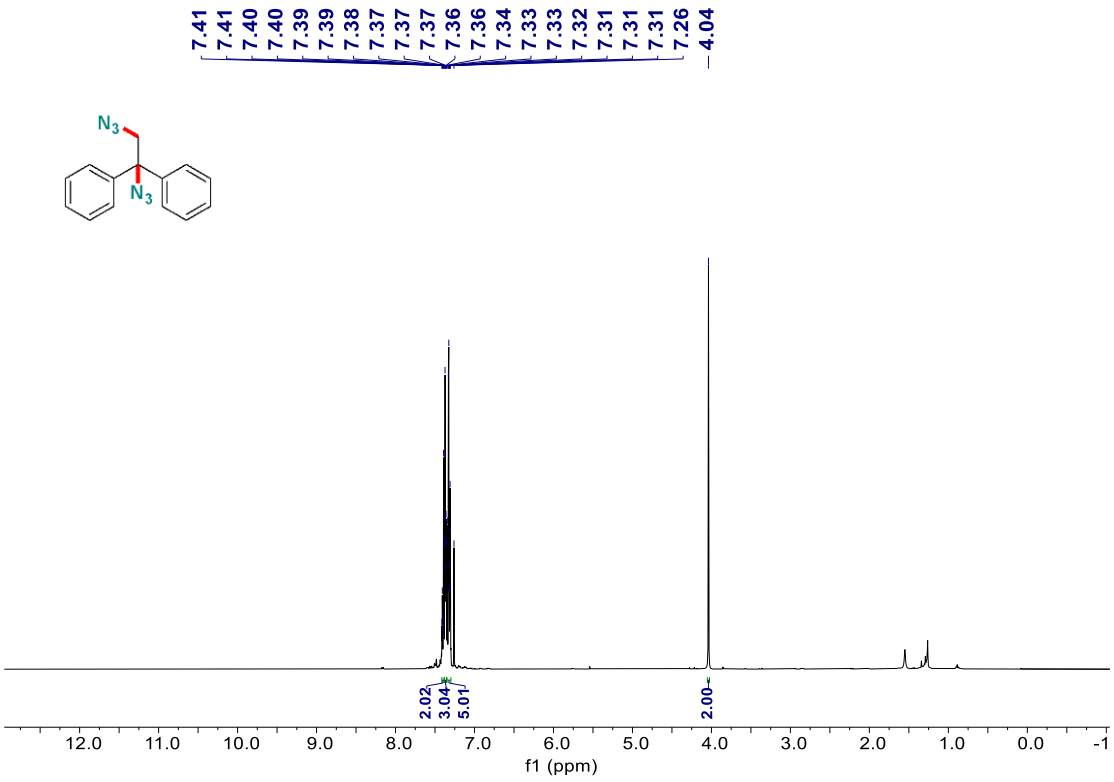
^{1}H NMR of compound **47** (500 MHz, $CDCl_3$)



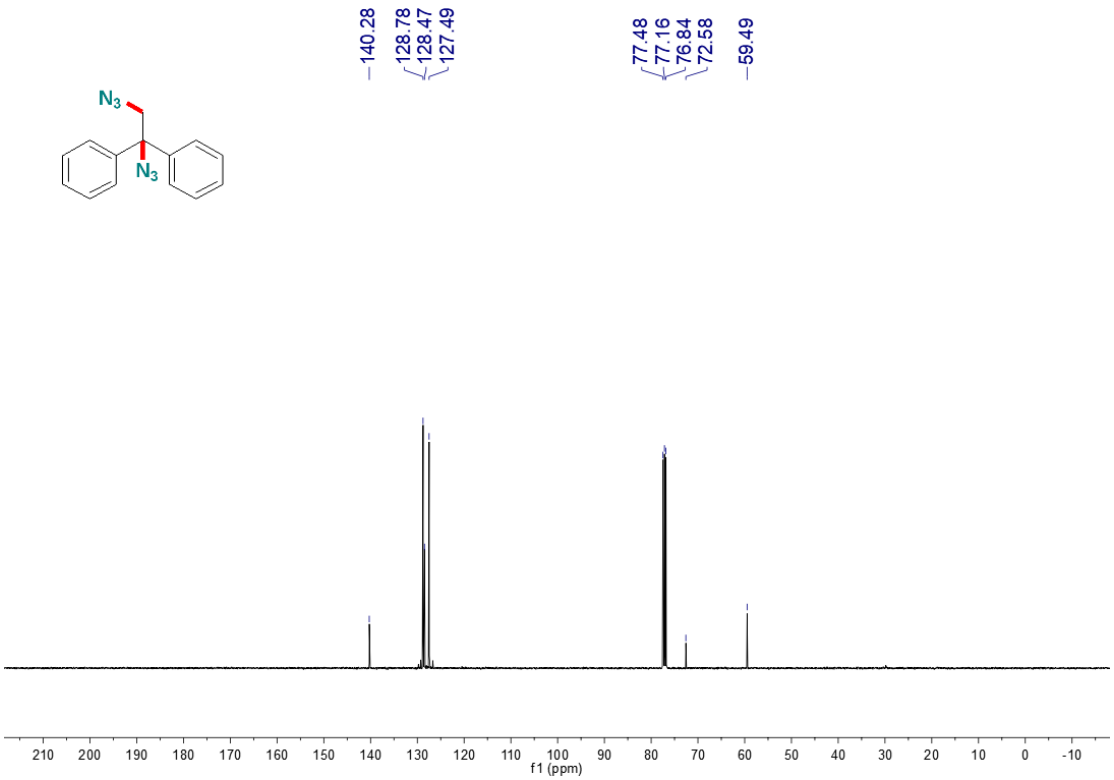
^{13}C NMR of compound **47** (126 MHz, $CDCl_3$)



^{1}H NMR of compound **1b'''** (500 MHz, $CDCl_3$)



^{1}H NMR of compound **48** (400 MHz, $CDCl_3$)



^{13}C NMR of compound **48** (101 MHz, $CDCl_3$)